THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

OCTOBER, 1907.

ORIGINAL ARTICLES.

THE ETIOLOGY OF TUBERCULOSIS.[1]

INFECTION THROUGH FOOD AND CONTACT. THE ALIMENTARY CANAL AS A PORTAL OF ENTRY FOR THE TUBERCLE BACILLUS.

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Historical. The possibility of tuberculous infection through the digestive tract appears to have been first pointed out by Klenke, who, in 1846, gave the clinical histories of 16 children who had been nourished on cows' milk, all of whom showed tuberculous lesions of the intestines, glands, skin, or bones. While his observations lacked scientific exactness, he deserves credit for calling attention to a method of infection which recent research has shown to be of quite frequent occurrence.

Chauveau, in 1868, published the first experiments proving the possibility of tuberculous infection through the alimentary canal, employing for this purpose young cattle reared in a region where tuberculosis was practically unknown. Further successful experiments, carried out on a larger number of animals, were reported by him in 1872 and 1873, establishing at this early day, for cattle at least, the important role played by ingestion in the transmission of tuberculosis.

Villemin, in 1869, published confirmatory experiments carried out on rabbits and guinea-pigs. He was the first to use a tube for the introduction of the tuberculous material into the stomach.

[1] An address delivered by invitation at the Fourteenth International Congress on Hygiene and Demography, Berlin, September 23–29, 1907.

The experiments of Gerlach, begun in Hanover in 1866, and later continued in Berlin on a much larger scale, gave the strongest support to the work of Chauveau. Gerlach was the first to experiment with the milk of tuberculous cows, and to prove that animals could be infected by the ingestion of such milk.

In 1870, E. Klebs reported experiments in which he had produced tuberculosis in animals by feeding tuberculous material from man as well as from animals, showing thereby the identity of the diseases. In 1873 he extended his experiments, employing tuberculous milk with positive results.

During the years 1870–73, Günther and Harms conducted at Hanover 94 feeding experiments, using animals of widely different species and tuberculous matter of various kinds. They obtained 24 positive and 70 negative or doubtful results.

Experiments with entirely negative results were reported by Colin, Semmer, and others. Those of Semmer were of especial importance. He fed upwards of 100 dogs on tuberculous material obtained from 30 cows, failing in every instance to produce tuberculosis. His results are at the present time interpreted as demonstrating the resistance shown by dogs to tuberculous infection.

Space does not permit me to go further into details, and I can only mention the admirable experiments of Viseur, Bollinger, Orth, Toussaint, Peuch, Baumgarten, Wesener, Leisering, Zürn, Saint-Cyr, Perroncito, Virchow and Schutz, Sydney Martin, Pearson, Schottelius, and others, all of which show that in animals infection takes place readily through the alimentary tract.

Many other facts, some experimental, some accidental, are at hand, confirmatory of the results above quoted. Among these may be mentioned the infection of large numbers of swine through feeding them milk from tuberculous cattle, one very striking instance of which has come under my personal observation in Pennsylvania. The spread of tuberculosis among swine and other animals through the use of skimmed milk and the waste products of creameries is also a well-established fact, and I believe that no one can seriously question the important role played by ingestion in the extension of the disease among the lower animals.

Many experiments have been carried out demonstrating the presence of the tubercle bacillus in various food products, such as milk, butter, etc., and the danger of such infected products for man has been generally recognized and accepted. In 1901, in his memorable London address, while discussing the relation of bovine tuberculosis to human health, Koch took the ground that infection through food could be assumed to have taken place with certainty only when the primary tuberculous lesion was located in the intestines. He claimed that this was rarely found to be the case, and argued that the danger of infection through food was slight.

The stand taken by Koch assumed that the tubercle bacillus was

unable to gain entrance to the system through the intestinal wall without the production of a lesion at the point of entrance. In the discussion of infection through food, we must, however, take into consideration the possibility of infection through every portion of the alimentary tract with which the food comes in contact, beginning with the mouth. It has been thoroughly proved that the tubercle bacillus is able to penetrate the mucous membrane of practically the entire alimentary canal, as well as that of other parts of the body. Experiments demonstrating this will be quoted when considering the various portions of the alimentary tract which may serve as portals of entry.

Mouth and Tongue, Palate and Gums. Tuberculosis of these structures is rare, even as a secondary manifestation in advanced phthisis, when all the parts are constantly exposed to large quantities of sputum containing myriads of tubercle bacilli. Experimental infection is readily produced, followed by enlargement and caseation of the related glands, but as primary avenues of entrance they play a minor part in the spread of tuberculosis.

Tonsils. The tonsils have long been believed to serve as portals of entry, not only for the tubercle bacillus, but also for many other pathogenic microörganisms. They are not infrequently the seat of primary tuberculosis, and often show scars and other changes attributable to tuberculosis. In man they are so situated as to come into contact readily with food as it is swallowed. They are also exposed to the secretions of the nose and nasopharynx as they pass backward into the œsophagus; hence they are liable to infection from food as well as from material primarily lodging in the nares.

The literature concerning infection through the tonsils is extensive, and I cannot even mention much that is of great value and interest. In the examination of tonsils removed from otherwise healthy persons, Krückmann found primary tuberculosis in 2 of 25 cases; Gottstein, in 2 of 20; Pluder and Fischer, in 5 of 32; and Scheibner, in 4 of 60 cases. Wood has collected from the literature 1671 cases, 88 (5.2 per cent.) of which showed primary tuberculosis. These examinations were made by various methods, and probably fall short of the truth. Lartigau and Goodale have shown that systematic inoculation of animals gives a higher percentage of tuberculosis. In 75 cases Lartigau found 12 (or 16 per cent.) tuberculous. Dieulafoy, by the inoculation of guinea-pigs, found tuberculosis of the tonsils in 15 of 96 cases. His work has been criticised on the ground that he made no histological examinations, and was not careful to exclude the crypts, which may lodge tubercle bacilli. However, Latham, who avoided these sources of error, in 25 consecutive autopsies on children from three months to thirteen years of age, found 7 which were tuberculous—results practically identical with those of Dieulafoy. Confirmatory reports have been made by a large number of observers, many of

which are included in the figures quoted from Wood. The susceptibility of the tonsils to tuberculous infection is shown by the examination of persons dead of phthisis.

Experimentally, the tonsils are readily infected, by direct application, as well as by feeding tuberculous material. In a series of experiments which I carried out at the laboratory of the State Live Stock Sanitary Board of Pennsylvania, swine fed with tubercle bacilli from man and from cattle developed generalized tuberculosis, with marked involvement of the tonsils, apparently primary, with necrosis and ulceration. Baumgarten observed, in his feeding experiments in 1884, that his animals showed primary tonsillar tuberculosis, with involvement of the related glands, and the same course was noted also by Orth in his studies. Woodhead traced tuberculous infection in swine from the tonsils into the neck, then into the thorax by the mediastinal and poststernal glands. Peira has shown that microörganisms are absorbed through the tonsillar epithelium, and, if virulent, may cause not only local disease, but be carried to the neighboring lymphatics, and thence to different parts of the body. Lexer confirmed these observations by a series of experiments on rabbits. Wood found that in swine the application of tubercle bacilli to the back of the mouth produced rapidly a primary tuberculosis of the tonsils, followed promptly by involvement of the submaxillary and cervical glands and extensive disease of the lungs. The mesenteric and bronchial glands were always diseased in about an equal degree. Aufrecht, by rubbing cheesy matter into the tonsillar region of rabbits, produced in one tuberculosis of the right tonsil and root of the tongue; in a second, tuberculosis of the cervical and mediastinal glands and the lung; in a third, disease of the mediastinal glands and the lung. All other organs remained free.

Grober concludes, from his thorough study of the question, that infection through the tonsil is the most frequent origin of apical tuberculosis. His experiments have demonstrated that from the cervical glands there is a direct route to the pleuræ and lungs, and that this leads especially to that portion of the lung most frequently the primary seat of tuberculosis—the apex. The evidence that the tonsils are frequently the portal of entry for the tubercle bacillus appears to me very conclusive, and it seems equally certain that food is the bearer of the infection in a large proportion of cases.

Pharynx and Œsophagus. Tuberculosis of the pharynx and œsophagus is extremely rare, and, as a primary affection, is practically unknown. It is probable, however, that the intact mucous membrane of the pharynx at times allows the passage of tubercle bacilli, which first show their presence by enlargement of the related glands. Experimental evidence of this is strong, though it must be borne in mind that it is always difficult to place the exact point of entry in the absence of any lesion. In the case of a monkey,

to which I fed tubercle bacilli enclosed in banana, and which died of pulmonary tuberculosis, the cervical glands were enlarged and caseous, though no lesion of the tonsils or neighboring parts could be found. It seemed probable that infection had taken place through some portion of the mouth or pharynx, though the tonsils may have been the point of entry.

STOMACH. There is no evidence that infection ever takes place through the stomach. Tuberculous disease of this organ is one of the rarest forms seen. The cause of this apparent immunity is not evident, but it is attributed to the protective action of the hydrochloric acid of the gastric juice. The action of the gastric juice on the tubercle bacillus has been the subject of considerable discussion and experiment. If this fluid had a germicidal effect on the tubercle bacillus, primary infection through the intestine would be manifestly impossible. It has been shown, however, that the tubercle bacillus is able to resist the action of the gastric juice for at least as long as the ordinary period of digestion.

INTESTINE. The intestine is very frequently involved in cases of phthisis, the autopsy reports of various pathologists giving figures that run from 30 per cent. to 90 per cent. In the great majority of these the lesion is unquestionably secondary, and due to swallowing sputum laden with tubercle bacilli. This does not, however, preclude the possibility that the pulmonary disease was caused in the first place by tubercle bacilli which gained entrance to the body through the intestine. In other words, the location of the primary lesion, on which so much stress has been laid, does not indicate with certainty the point of entrance of the invading organism. This appears to be especially true in children, in whom tuberculosis tends to become rapidly generalized.

The susceptibility to infection through the intestine unquestionably varies with the age of the individual. In young children the intestinal epithelium is looser, more delicate, and softer than in later life; the mucous membrane contains more fluid, and is more liable to slight injury (Furst). The intestinal catarrhs to which children are so liable also tend to lessen the natural resistance of the mucosa to invasion by microörganisms. Even before the discovery of the tubercle bacillus Weigert called attention to the permeability of the intestinal mucosa of young children to the virus of tuberculosis, stating that the mesenteric glands might be markedly swollen and cheesy, while the mucosa and lymph vessels showed no change whatever.

Tuberculosis of the mesenteric glands without lesion of the intestinal mucosa was observed also by Cohnheim, and since by von Bollinger, Wesener, Heller, Kossel, Aufrecht, von Hansemann, Rilliet and Barthez, Widerhofer, and many others. McFadyean and McConkey, by the inoculation of animals, demonstrated the presence of tubercle bacilli in 25 per cent. of children examined

who showed no lesion of the intestine. Rabinowitsch also has shown that the mesenteric and bronchial glands of children, as well as of adults, may contain living tubercle bacilli, though there had been no clinical sign of disease and the microscope gave negative results. In his feeding experiments, Orth produced tuberculosis of the mesenteric glands without change of the intestine. Feeding with perlsucht material caused tuberculosis of the various organs without perceptible lesion of the intestine or peritoneum.

PRIMARY INTESTINAL TUBERCULOSIS. Pathologists give the most contradictory reports as to the frequency of primary intestinal tuberculosis. It is impossible to explain satisfactorily the widely differing findings, coming, as they do in some instances, from hospitals in the same city. They are accounted for in part by differences in the methods of examination and interpretation of findings; in part, by the class of patients frequenting certain hospitals; and in part by a real difference in the incidence of intestinal infection in various communities, brought about by local customs and habits. In all reports a large percentage of cases is found in which it has been impossible to determine the site of the primary lesion, and from many of them it is difficult to draw correct conclusions, since they have been compiled to demonstrate certain points, and do not give clear details as to other important features.

From England only do we get statistics which approach uniformity. English pathologists who have studied tuberculosis in children are practically unanimous in believing that infection through the intestine is of frequent occurrence. Still, Shennan, Symes and Fisher, Guthrie, Carr, Ashby, Batten, and Kingsford report on 1560 autopsies on children in which the primary lesion was found in the intestine 290 times, or in 18.6 per cent. of all cases. These were seen in different parts of England, though the largest number came from London. Woodhead, in 127 autopsies on children, found the mesenteric glands involved 100 times; in 69 the bronchial glands were also involved; in 27 the bronchial glands alone, and in 14 the mesenteric alone.

In the United States of America, Northrup, Holt, and Bovaird report on 369 cases, all from New York or its environs, with only 5 of intestinal origin—a little more than 1.3 per cent. Holt contributed 119 of these autopsies, in none of which did he consider the intestine the seat of the primary lesion. It is interesting to note, however, that he found the mesenteric nodes involved in 35 per cent., and the intestines in 37 per cent. of these cases. From the Children's Hospital of Philadelphia, Hand reports 115 autopsies, with 10 cases (8.7 per cent.) of primary intestinal localization, and 1 of tonsillar invasion. In 29 cases the point of invasion could not be determined.

In this connection the work of Councilman, Mallory, and Pearce is most instructive. They found tuberculosis in 35 of 220 children

dead of diphtheria. In 18 of these the mesenteric lymph nodes were tuberculous, with involvement of the intestine 6 times; and in 7 cases the mesenteric glands were diseased without involvement of any other part of the body. In 13 cases (37.1 per cent.) the infection was evidently through the digestive tract.

The statistics from Germany are most contradictory and confusing. As is well known, Koch considers primary intestinal tuberculosis very rare, having collected only some 28 cases. Before accepting a case as being due to food, Koch demands a train of evidence, as follows: Clinical and anatomical data of the disease and its point of invasion; the exclusion of all other sources of infection; the coincident infection of others using the same milk; demonstration of udder tuberculosis in the cow furnishing the milk. It is needless to say that such a train of proof is practically impossible to obtain. Furthermore, neither Koch nor anyone else asks for such evidence in determining the source of respiratory tuberculosis—or, in fact, of any other disease.

Baginsky, in a series of 806 autopsies, 144 of which showed tuberculosis, found only 6 in which he considered the intestinal lesion the oldest. In a second series of 933 autopsies on children he did not once find intestinal tuberculosis without involvement of the lungs and bronchial glands. This statement does not appear to me to be of much value, since no indication of the site of the primary lesion is given. Biedert found only 16 cases of primary intestinal tuberculosis in 3104 autopsies on children. Widerhofer, Heubner, Benda, von Hansemann, Ganghofner, and others agree in regarding primary intestinal tuberculosis as comparatively infrequent. Von Hansemann saw only 25 cases in seven years. Widerhofer, in an analysis of 418 cases of tuberculosis in children, found involvement of the intestine (not primary) 101 times. Of these 43 (42.5 per cent.) were between the ages of two and five years, when food infection is most liable to occur.

On the other hand, we have a mass of testimony from equally competent observers which agrees closely with the figures from England. Hueppe, while giving no statistics, says: "The number of cases (primary intestinal infection) may fairly be reckoned as between 25 and 35 per cent. of all deaths in children from tuberculosis." Hof, in a systematic study of the autopsy records of the Pathological Institute at Kiel, found 2697 cases of tuberculosis in adults, 159 (5.9 per cent) of which were primary in the intestine; while in 84.9 per cent. the respiratory tract was primarily involved. In children there were 936 cases of tuberculosis, 235 (25.1 per cent.) of which showed evidence of infection through the intestine, and 527 (56.2 per cent.) respiratory infection.

Wagener, in 600 autopsies, 76 of which were on children, found primary intestinal tuberculosis in 16 to 21 per cent. Heller, among 714 fatal cases of diphtheria, found tuberculosis 140 times, in 53

(37.8 per cent.) of which the origin was primary in the intestine. In a later series of autopsies Heller found intestinal tuberculosis in 12 per cent. of the adults and 26 per cent. of the children. Nebelthau, in 26 autopsies on tuberculous children at the Halle Polyclinic, found the infection was primary in the intestine in 5 (19.2 per cent.), and in the respiratory tract in 9 (34.6 per cent.), while in 12 (46.1 per cent.) both tracts were infected. Kossel, in 14 children dead of other diseases, found tuberculosis of the bronchial glands 10 times, and of the mesenteric glands 4 times. In 22 children who died of tuberculosis, only once did he find the disease confined to the intestine. Lubarsch, in 297 autopsies on children, found tuberculosis in 63, of which 14 (21.2 per cent.) were primary in the alimentary tract.

The marked differences in the findings of pathologists even in the same city has been mentioned. In Berlin, von Wagener, at the Bethanien Hospital, from October, 1903, to October, 1904, found in 67 autopsies on children from one to fifteen years old, primary intestinal tuberculosis in 16 per cent., while at the Charité, from October, 1902, to December, 1903, Orth found in 131 children only 1.5 per cent. of undoubted primary intestinal and mesenteric disease. Edens, among 31 tuberculous children at the Bethanien Hospital, seen from October, 1904, to October, 1905, found 35.5 per cent. of primary intestinal disease, while Orth during the same years found only 8 per cent. in 77 children (Rabinowitsch). At the same hospital, from October, 1905, to October, 1906, Edens found 18 cases of primary intestinal tuberculosis in 409 autopsies, at all ages. Of the 74 children from one to fifteen years old, 21 of whom were tuberculous, 10 (47.6 per cent.) showed primary intestinal involvement. Of 319 cases from fifteen to ninety years old, 130 were tuberculous, and 8 (6.2 per cent.) showed primary intestinal involvement.

In Copenhagen, Febiger found 13 cases of tuberculosis beginning in the intestine among 213 autopsies on persons of all ages, or 6 per cent. for all cases and 11 per cent. for tuberculous cases. Ipsen carried on the work, and gives us a series of 600 autopsies, including those of Febiger. In 32 cases primary tuberculosis of the digestive canal was found, which gives 5.3 per cent. for all cases and about 10 per cent. for tuberculous ones. These figures include 102 children from birth to fifteen years of age who died from various diseases. Among these 6 showed tuberculosis limited to the intestine.

Harbitz gives the following results obtained from the examination of 117 cases: Primary in the respiratory tract, 48 (41 per cent.); primary in the digestive tract, 26 (22 per cent.); primary in the digestive or the respiratory tract, 24 (20.5 per cent.); general lymph-node tuberculosis, 11 (9.4 per cent.); doubtful, or other primary seats, 8 (6.8 per cent.).

Studies on the bodies of children who have died of diseases other than tuberculosis, such as those reported by Councilman, Mallory, and Pearce, Heller, and Kossel, are particularly valuable in the determination of the avenue of entry for the tubercle bacillus. The disease tends to become generalized so rapidly in children that at autopsy it is often impossible to tell by what route infection occurred. When death has been due to other causes the tuberculous lesion is usually localized, and often confined to the glands in relation to the point of invasion; hence the portal of entry can be determined with great certainty.

Statistics of Primary Intestinal Tuberculosis. Furst has collected the reports of 124 cases of undoubted primary intestinal tuberculosis, 30 almost certainly primary, and 23 doubtful ones. He concludes that there are on record some 160 cases of primary intestinal involvement which cannot be questioned. To these we may add 18 recently reported by Edens, and about 20 of which I have knowledge, including the cases published by Northrup, Holt, Bovaird, Hand, Ravenel and Fife, and some unpublished ones. Furst leaves out of consideration entirely the 290 cases given by the English pathologists quoted above.

The total, however, is not large when we consider the enormous death rate from tuberculosis. Numerous experiments long ago convinced me that an infection through the alimentary canal often shows itself first in the thorax; and I believe it is unfair to consider as cases of intestinal infection only those in which the primary lesion is found in the intestine or mesenteric glands. The question hinges largely on the ability of the tubercle bacillus to pass through the intestinal wall without causing a lesion at the point of entrance, and this will be next considered.

Permeability of the Intestinal Wall. It is believed by many pathologists that the tubercle bacillus is able to penetrate the normal mucous membrane of the intestine without leaving any lesion at the point of entrance. In fact, this seems to be true of the mucous membrane of other parts of the body also, as shown by the great frequency with which the various groups of glands are found to be tuberculous with no demonstrable lesion of the surfaces they drain. In 1000 swine, infected through food, Ostertag found the glands of the throat, neck, and mesentery tuberculous, while the mucous membrane of the intestine was always free from disease. The passage of tubercle bacilli through the intestine appears to be most likely to occur during the digestion of fats, as shown in the experiments given below.

Von Baumgarten has recently denied that tubercle bacilli penetrate the body membranes without causing a lesion at the point of entry. In the numerous experiments by himself and his students he has found that animals fed with milk containing tubercle bacilli developed an intestinal tuberculosis with general infection. If the

infection was rapidly fatal the intestinal lesions were very small, being found only in sections, but widespread. The mesenteric glands showed more advanced disease and, apparently, of longer duration. In aspiration tuberculosis also he has not been able to discover disease of the lymph glands without involvement of the trachea or lungs. Von Hansemann accounts for cases of abdominal infection without intestinal lesion on the ground that a slight tuberculosis of the intestine may disappear, leaving no sign of its location. The truth of this observation must be admitted, but it does not explain the numerous experiments in which the tubercle bacillus, as well as other organisms, have been shown to penetrate the intestinal wall in the course of a few hours even when there is no demonstrable lesion.

Orth, in 1879, and Cornet, in 1880, observed bacilli pass step by step through the fully developed mucous membrane of the uninjured intestine and reach the lymph channels and mesenteric glands, leaving no recognizable trace behind (Furst). Dobroklonski, in 1890, working under Cornil, showed that the tubercle bacillus would quickly penetrate the healthy wall of the intestine in guinea-pigs. Desoubry and Porcher, students of Nocard, showed in dogs that during the digestion of fats large numbers of bacteria were carried through the intestinal wall and could be detected in the chyle within a few hours after the meal was given. If food free from fat was given few or even no bacteria could be found. Nicolas and Descos, in 1902, found that tubercle bacilli given to dogs in fatty food reached the chyle within three hours. During feeding experiments conducted at the laboratory of the State Live Stock Sanitary Board of Pennsylvania, we frequently observed extensive tuberculosis of the lungs and thoracic glands in animals which showed slight or even no involvement of the intestine. In 1902-3, I introduced into the stomachs of a number of dogs tubercle bacilli suspended in an emulsion of melted butter and warm water, using a tube in order to prevent possible infection through the trachea. The dogs were killed after three and one-half to four hours, during active digestion, as much chyle as possible was collected, and the mesenteric glands were removed. Guinea-pigs were inoculated with this material. Tubercle bacilli were demonstrated in abundance in 8 of 10 experiments. The dogs were kept on soft food for some days before the experiments, and were purged with castor oil, in order to rid the intestine of all foreign matter which might injure the mucous membrane. Numerous sections of the gut were examined also, but no injury could be detected. Römer and von Behring have shown that the tubercle bacillus, and even the anthrax bacillus, which is very much larger, passes readily through the intestinal mucosa of young guinea-pigs. A single feeding with a minute dose of tubercle bacilli frequently produced infection, the glands of the neck always being involved, and later there frequently developed a type of disease

usually regarded as the expression of an inhalation tuberculosis. As is well known, von Behring believes that the origin of epidemiological tuberculosis in man and epizoötic pulmonary tuberculosis in cattle is a primary intestinal infection taking place in early life.

The subject has been recently studied by Calmette and his fellow-workers Guérin, Vansteenberghe, and Grysez. In numerous experiments they have found it impossible to produce anthracosis of the lungs even when animals were compelled to breathe an atmosphere saturated with lamp-black, provided the œsophagus was closed. On the other hand, when lamp-black was introduced into the stomach by means of a tube, or mixed with food, anthracosis of the lungs appeared rapidly. When tubercle bacilli, dry or moist, were administered by inhalation, by intratracheal insufflation, or by direct inoculation into the trachea, the bacilli never penetrated farther than the first branches of the bronchi. The introduction of tubercle bacilli into the stomach through a tube, in order to avoid danger of respiratory infection, always produced tuberculosis rapidly. They confirm the observation that tubercle bacilli readily penetrate the intestinal wall without leaving a lesion. They have traced the bacilli, and find that as soon as they reach the chyle vessels they are taken up by the leukocytes, which, from this time, act as carriers and convey them to the related glands, where they are retained for a longer or shorter time, reaching finally the thoracic duct, and through it the circulation. In young animals the mesenteric glands retain the leukocytes with their englobed bacilli for some time, the glands enlarging in proportion to the intensity of the infection, the lungs becoming involved secondarily. In the adult the glands do not retain the bacilli nearly so long, and they can be detected in the lungs twenty-four hours after their introduction into the stomach. Calmette concludes that pulmonary tuberculosis acquired at any age may be due to recent intestinal infection.

Besanti and Panisset have shown that tubercle bacilli given to dogs suspended in soup reach the blood of the heart within four to five hours. In 4 out of 6 experiments they obtained positive results. Bartel found that after a single dose tubercle bacilli penetrated the uninjured intestine and reached the mesenteric glands during the following digestive period. Von Weismayr, as the result of his studies, is of the opinion that microörganisms can penetrate the intact intestinal wall, and be carried by the lymph cells through the lymph channels to the related glands. Schlossman and Engel have shown that when tubercle bacilli suspended in milk or cream are injected into the stomachs of young guinea-pigs through an incision in the abdominal wall they reach the lungs within six hours, as shown by killing the animal and inoculating portions of the lungs into other pigs.

Infection by Bovine Tubercle Bacilli. In 1901, I isolated from the mesenteric glands of a child who died of tuberculous men-

ingitis following primary intestinal infection, a culture (B B) which, after the first generation, showed all the characteristics of the bovine bacillus, killing cattle rapidly. A second culture (U) also from a case of meningitis, though of doubtful origin, was of the human type in growth and morphology, but showed high virulence for dogs and calves. A third culture (K K), reported by Dr. Fife and myself from a case of primary intestinal tuberculosis, was bovine in all respects, including virulence for calves. In America, de Schweinitz has isolated bacilli of the bovine type from children three times; Theobald Smith, once; and Mohler, once. In Europe, Febiger and Jensen, Wolff, Westenhoffer, the Commission of the Imperial Board of Health, and the English Royal Commission have isolated from cases of human tuberculosis bacilli of the bovine type, fully virulent for cattle. The German Commission examined 56 cultures from man, and found 6 (10 per cent.) to be bovine. These were, with one exception, from children with mesenteric or intestinal lesions. The English Commission studied 60 cultures isolated from man, of which 14 (23 per cent.) proved to be of the bovine type; 28 of the cases from which these cultures were obtained had histories pointing to intestinal infection, and of these 13 (46.4 per cent.) gave cultures of the bovine type.

The opportunities for the inhalation of the bovine tubercle bacilli by human beings are slight, except, perhaps, for persons who habitually care for cattle, and, compared to those for ingestion, are insignificant. There is practically no possibility for the inhalation of bovine bacilli by children even if we admit that the aspiration of particles of food may occur. We are, therefore, justified in concluding that in those cases from which the bovine bacillus has been isolated the infection has taken place through the digestive tract.

Infection through Contact. It is impossible to state how frequently contact is concerned in the spread of tuberculosis. In the great majority of cases of infection by this means the source is never suspected. Contact plays an important part in the spread of many other diseases, and is probably more frequently the mode of infection in tuberculosis than we believe. Kissing of infants by tuberculous parents is especially dangerous, as is also the habit, common among mothers and nurses, of tasting the infant's food in order to test its heat. Demme recounts the case of a tuberculous nurse who fed her charges with a spoon she constantly put into her own mouth, with the result that four died with primary isolated intestinal tuberculosis.

The hands of consumptives are frequently contaminated with sputum and excretions. Baldwin showed, by the inoculation of guinea-pigs with the washings from the hands of 10 private patients, that 8 were the bearers of living tubercle bacilli. Of 5 sanatorium inmates, only 2 gave positive results. Children playing on floors soiled with sputum may readily get their hands

contaminated, and thus convey bacilli to their mouths. The hands also become contaminated by means of handkerchiefs, rags, sputum cups, clothing, bedding, etc., used by consumptives. Local infections have been observed through the use of towels, handkerchiefs, and other articles, and in the laundering of such articles. Wounds or abrasions on the hands, face, and other parts of the body are liable to become infected through soiled bandages or tuberculous attendants, as in cases reported by Verneuil, Tuffier, Kraske, Wahl, and others. Elsenberg observed infection of the penis after circumcision by a tuberculous priest, who used his mouth to arrest bleeding. Similar observations are recorded by Meyer, von Lehman, and Hofwokl.

Inoculation of the hands through wounds is often seen, chiefly among physicians and veterinarians engaged in postmortem work on man and animals. It occurs also in butchers and others handling tuberculous carcasses. The usual result of such inoculation is the anatomical tubercle, though tuberculosis verrucosa cutis sometimes follows, especially in those handling animal products. Such cases have been reported by Gerber, Lassar, Spronk and Höfnagel, Pfeiffer, Tscherning, Krause, Joseph and Trautman, Schutz, Kliene, de Jong, Mueller, Hartzell, Ravenel, and many others. In the great majority of such cases the infection remains more or less local, and the health does not suffer. In some it becomes generalized and death follows, as in the cases of Pfeiffer and Hartzell. The death of Wally, principal of the Royal Veterinary College of Edinburgh, was attributed to such an infection from a bovine source, and it is well known that Laennec believed that his phthisis originated through a postmortem wound. The proof in none of these cases is entirely conclusive. Among other modes of infection through contact which have been reported may be mentioned the bites of consumptives (Verchère, Jeanselme); vaccination; skin transplantation (Czerny); rubbing with phthisical saliva during tattooing (Jadasohn); the use of milk as a soothing application to injuries, etc. Such methods are exceptional, and are of little importance in spreading the disease.

Sources of Infection. The scope of this paper does not permit me to discuss this topic at length. It has been repeatedly proved that the tubercle bacillus passes into the milk of tuberculous cows even when there is no disease of the udder (Smith, Rabinowitsch and Kempner, Ravenel, and others), and, further, that tuberculosis is communicable from animals to man. The chief source of infection through food, strictly speaking, must then be considered the milk and other products of tuberculous cattle. However, food may become contaminated by sputum and excretions from consumptives. Our honored president has clearly demonstrated the danger from droplets expelled during coughing, sneezing, etc. Acting on the suggestion contained in his work, I have

shown that cows throw out many tubercle bacilli in the same way. These floating particles, as well as the dust of dried sputum, are drawn into the nose and mouth during inspiration, and pass into the œsophagus with the secretions which are constantly swallowed, thus gaining access to the alimentary canal.

CONCLUSIONS. 1. The alimentary tract is a frequent portal of entry for the tubercle bacillus.

2. The tubercle bacillus is able to pass through the intact mucous membrane of the alimentary tract without producing a lesion at the point of entrance. This takes place most readily during the digestion of fats.

3. The bacilli pass with the chyle through the lacteals and thoracic duct into the blood, which conveys them to the lungs, where they are retained largely by the filtering action of the tissues.

4. Infection through the alimentary tract is especially frequent in children.

5. Milk from tuberculous cows is the source of infection in many cases. Our present knowledge does not enable us to state the exact proportion of cases of tuberculosis due to this cause, but it is probably considerable.

6. Tuberculosis can be communicated by contact, such as kissing, soiled hands, accidental injuries in postmortem work, or during the cleansing of vessels used by consumptives, etc. These modes of infection play a comparatively small part in the dissemination of the disease.

THE ETIOLOGY OF CERTAIN CASES OF LEFT-SIDED INTRA-ABDOMINAL SUPPURATION—ACUTE DIVERTICULITIS.[1]

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DURING the past ten years I have observed six cases of acute intra-abdominal abscesses, all originating in the left lower quadrant and presenting symptoms so similar to acute appendicitis as to lead me to consider the possibility of transposition of the viscera.

The first of these cases occurred at the New York City Hospital. A middle-aged woman was admitted to the surgical ward, suffering from pain, tenderness, and muscular rigidity in the left inguinal region. The history of the onset of the symptoms was difficult to obtain, but as she regarded the condition as one of acute indigestion, it is probable that it was sudden in its onset, and in the beginning it was associated with nausea and vomiting. When first seen by me there was moderate fever, some acceleration of the pulse, and, on

[1] Read at a meeting of the American Surgical Association, Washington, D. C., May 9, 1907.

careful palpation, a well-defined mass could be felt occupying a position midway between the left anterior superior spinous process and the median line. Operation revealed a well walled-off intraperitoneal abscess, containing about 100 c.c. of foul-smelling pus. There was no escape of gas, and no evidence of a fistulous opening; in fact the intestines were so matted together with fibrinous exudate that they could not be recognized, and no effort was made to separate them. The wound was closed with drainage, and she made a rapid and satisfactory recovery.

My second case was also seen at the New York City Hospital. An elderly woman was admitted suffering from pain, tenderness, muscular rigidity, and a mass in the left inguinal region. These symptoms had been present for several days. On admission, she had a slight elevation of temperature and looked moderately septic. The indurated area in this case was situated somewhat nearer the iliac spine, but in all other respects it clearly resembled the case just reported. On operation the peritoneal cavity was apparently not opened, the incision, which was quite near Poupart's ligament, leading directly to a large abscess cavity, which contained perhaps 250 c.c. of thick pus. The cavity, which was freely explored through a large incision, was seen to extend inward, beneath the descending colon and upper part of the sigmoid, the under surface of the latter apparently forming a part of the roof of the cavity. The bowel wall at this point was covered with a thick, fibrinous exudate, and it was thought by several who saw it that there might have been a small perforation, which had been closed by the exudate. After evacuating the pus the wound was partly closed and the cavity packed with sterile gauze. She made a slow but satisfactory recovery.

In both of these cases my records are imperfect, and I am obliged to rely largely upon my memory, but I distinctly recall that the cases made a strong impression upon my mind, and that I discussed their possible etiology with several of my colleagues. In the beginning I was strongly in favor of the belief that we had to do with a transposition of the viscera and a left-sided appendicitis. In my second case, however, this theory was easily disproved, as we had a retroperitoneal abscess, which, if it had been caused by a perforated appendix, would certainly have shown some trace of the organ by our careful inspection. My final conclusion was that in all probability the infection took place through some very small perforation of the sigmoid, as from a fish bone or other pointed foreign body, or possibly through a small area of necrosis occurring in a dysenteric or tuberculous ulcer.

My third case was observed three or four years later, at the Roosevelt Hospital. A man, sixty years of age, was admitted to the hospital with a diagnosis of abdominal tumor. On questioning him we elicited the fact that he had always enjoyed fair health, but

had been constipated for a number of years. Four weeks before his admission he had complained of more or less severe abdominal pain, which had prostrated him and compelled him to take to his bed. This continued for several days, and, he thought, was associated with some fever. As the pain and fever subsided he noticed a painful swelling in the left inguinal region, which gradually increased in size until his admission to the hospital, when it was as large as a small cocoanut.

On examination, there was practically no muscular rigidity. Inspection revealed an oval mass midway between the umbilicus and the anterior spine of the ilium on the left side. This mass was flat on percussion, somewhat movable, smooth on the surface, of the density of an ovarian cyst, and was elastic but not frankly fluctuating. The tenderness to pressure was so slight as strongly to suggest a new-growth rather than an inflammatory mass. This view was also strengthened by the absence of fever.

Under ether anesthesia an exploratory incision was made through the left rectus muscle. The subperitoneal fatty tissue was œdematous. On dividing the peritoneum the incision opened into a large abscess cavity, which contained about 500 c.c. of creamy, odorless pus. The wall of the cavity was made up of omentum and several loops of intestine, all matted together with a dense, fibrinous exudate. The cavity of the abscess was washed out, the wound partly closed by layer sutures, and a large drain inserted at the upper angle. He made a satisfactory convalescence.

This case, while it cast no additional light on the etiology of this condition, served to reawaken my interest in the subject. About this time, in discussing the subject with my colleague, Dr. Evan Evans, he suggested as a possible cause, the rupture of a small acquired diverticulum of the sigmoid or descending colon. These diverticula are of fairly frequent occurrence in elderly people, are generally multiple, and, on account of their thin walls, might easily rupture if inflamed or distended by a foreign body. I, therefore, made a systematic inquiry of a number of pathologists of my acquaintance, who were making large numbers of autopsies; and, while most of them had seen these diverticula, occasionally present in large numbers, none could recall an instance in which rupture had occurred as a result of pressure of a foreign body or an inflammatory process.

Intestinal diverticula, as is well known, are divided into two general classes—the congenital and the acquired. The most frequently observed type of the congenital variety is the one known as Meckel's diverticulum. As recently described by Léon Cahier,[2] in his admirable essay upon the subject, a Meckel's diverticulum possesses

[2] L'inflammation des diverticules intestineaux ou diverticulite, Revue de chirurgie, September, 1906.

the following characteristics: It is single; it has a rectangular implantation into the free border of the terminal portion of the ileum, generally in the neighborhood of the ileocecal valve; it is made up of all of the coats of the intestine; it is generally more than 2 cm. in length; and it has a terminal filament which may be free or attached to the abdominal wall, the mesentery, or another part of the intestine. The acquired diverticula, on the other hand, are, as a rule, multiple, small, thin-walled, and round or ovoid in shape; they may be found in any part of the intestinal canal, but are more frequent in the left colon and the rectum, and are in reality hernial protrusions of the mucous membrane through the separated fibers of the muscular coat.

While congenital diverticula have been known since the early part of the eighteenth century to be the not infrequent cause of intestinal strangulation, and during the last fifty years to be the occasional cause of peritonitis from perforation, the pathological importance of the acquired diverticula in the production of intra-abdominal abscess has been practically ignored by clinicians, and barely mentioned by pathologists. Wallmann,[3] in 1858, reported 9 cases of acquired diverticula of the colon, of which 1 was in the ascending portion, 3 in the transverse, 3 in the descending, and 2 in the sigmoid. In no instance, however, was any other pathological lesion present. Leube[4] has described these diverticula as hernias of the mucous membrane, and stated that they occur most frequently along the mesenteric border of the bowel. Klebs called attention to the relationship between these protrusions and the bloodvessels of the bowel. In 1900 Hodenpyl[5] exhibited to the New York Pathological Society two specimens of acquired diverticula, one of the duodenum and one of the colon. The latter (see figure) presented seventy-nine distinct pouches, the majority being in the lower segment of the gut. He expressed the opinion that they were probably due to internal pressure caused by chronic constipation. Other interesting communications on the subject have been made by Max Edel[6] and Graser.[7]

Regarding the pathological importance of these diverticula, I have been able to glean very little from the literature. Sydney Jones,[8] in 1858, was, perhaps, the first to mention it. He described a case of intestinal-bladder fistula, which, he believed to be due to ulceration of a sigmoid diverticulum. Loomis,[9] in 1877, described a case of peritonitis due to inflammation of multiple diverticula of the left colon, several of which contained concretions. Birch-Hirschfeld,[10] in 1887, called attention to the possibility of diverticu-

[3] Virch. Arch., 1858, xiv.
[4] Ziemssen's Spec. Path. und Therapie.
[5] Trans. New York Path. Soc., March 29, 1900.
[6] Virch. Arch., 1894, cxxxviii.
[7] Münch. med. Woch., 1899, Nr. 22, and Arch. f. klin. Chir., 1899.
[8] Trans. Path. Soc. London, 1858.
[9] Trans. New York Path. Soc., 1877.
[10] Path. Anat., 1887.

litis with perforation and the formation of intra- or extra-peritoneal abscess. George Biggs,[11] in 1894, reported to the New York Pathological Society a specimen showing multiple diverticuli of the sigmoid, one of which had perforated and caused an extraperitoneal abscess. More recently Fischer[12] has reviewed the entire subject, described four specimens, and expressed some doubt regarding the role of constipation as a causative factor. The most satisfactory and comprehensive exposition of both the pathological and clinical aspects of the subject is the paper by Edwin Beer, in the AMER. JOUR. MED. SCI., July, 1904, p. 135.

Hodenpyl's specimen of multiple acquired diverticula of the colon (sigmoid flexure).

It will thus be seen that from time to time during the past half century pathologists have observed and reported specimens showing inflammation, necrosis, and perforation, with or without the presence of fecal concretions, of these false diverticula of the left colon, and have clearly demonstrated the relationship between these lesions and a general or localized peritonitis. For the most part, however, these communications have been buried in the transactions of pathological societies or have appeared in periodicals not largely read by clinicians. This circumstance and the rarity of the condition will easily account for the fact that the disease is not

[11] New York Path. Soc., March 28, 1894. [12] Jour. Exp. Med., 1900, p. 333.

described in our clinical text-books, nor generally recognized by the profession.

I have long been impressed with the probable relationship between these diverticula and left-sided abdominal abscess, but have been unable to verify this impression until quite recently. The following case, while it does not prove the relationship absolutely, presents features which render it highly probable:

F. M., aged forty-seven years, was seen by me in consultation in August, 1906. The patient for twenty years had been a high liver and a hard drinker. One year before, he had had an attack of acute nephritis with uremia, from which he had partially recovered. Six weeks before being seen by me he had experienced an attack of abdominal pain, with nausea and vomiting. The pain was at first located in the centre of the abdomen, but later shifted to the left lower quadrant. There was moderate fever and considerable prostration during the first few days following the onset of the symptoms. Later, a tender swelling was noticed just to the left of the median line, and below the umbilicus. This mass slowly increased in size, and at times would be so painful as to interfere with sleep. The symptoms were only of moderate severity, however, and he remained under medical treatment for several weeks in the country, until increased fever, chilly sensations, and augmented tenderness in and about the mass led his medical adviser to advocate his removal to a hospital. He was accordingly brought to New York and placed under the care of my colleague, Dr. E. B. Shelby, with whom I saw him in consultation on the following day.

At my first examination I found the patient with a temperature of 100°, pulse 110. He complained of no discomfort except when moved about or palpated. On inspection, a swelling could be distinctly seen below and to the left of the navel. On palpation there was slight rigidity of the left rectus muscle, and an oval mass about the size of an egg-plant could be felt, which was distinctly tender to pressure. The appendix region was free from tenderness. The free border of the liver could be felt well below the costal arches; the spleen was large to percussion, but could not be palpated. The blood showed a moderate leukocytosis, with an increased percentage of polynuclear leukocytes. The heart and lungs were negative. The urine showed a trace of albumin with casts, but was sufficient in quantity.

He was removed to the Roosevelt Hospital, where, under general anesthesia, an incision was made through the outer border of the left rectus muscle, which exposed a large, well walled-off abscess, containing gas and about 500 c.c. of foul-smelling pus. On account of the poor physical condition of the patient, no effort was made to break up adhesions, with the view to determining the point of intestinal leakage.

He rallied well from the operation and made a tardy convales-

cence. The wound healed very slowly; one small sinus persisted and led downward toward the pelvis, and through it small quantities of gas would occasionally escape. On three or four occasions during his convalescence secondary abscesses formed in the neighborhood of the sinus. These, as a rule, discharged spontaneously. He was up and about, however, and after October 1 was able to go down town and attend to his business.

Later, as his health improved, an attempt was made to find and close the intestinal opening. On December 5, under ether anesthesia, after evacuating and packing an abscess of the abdominal wall, the sinus was followed down to the region of the sigmoid flexure in the pelvis, without opening the peritoneal cavity. A second incision was made to the right of the median line and the peritoneal cavity was opened and explored. The intestines were generally free from adhesions. Two portions of the gut, however, were firmly adherent to the wall of the abscess; the first, which in all probability was the primary lesion, was situated about the middle of the sigmoid; the second, probably a secondary communication, was a loop of small intestine adherent to the upper part of the abscess wall above and to the left of the umbilicus. Both of these adhesions were separated, and the minute openings closed with purse-string sutures. The right abdominal wound was united by layer sutures; the wound on the left side exposing the abscess cavity was partly united and drained with gauze. The patient bore the operation well, but vomited a good deal after coming out from the ether. There was practically no reaction during the first twenty-four hours, the temperature and pulse remaining at or near the normal. The vomiting, however, was troublesome, and on the second day after operation he vomited a large quantity of dark fluid, with clotted blood, which greatly weakened him, and was followed by a rapid rise in pulse and temperature. The vomiting was repeated several times, and eventually resulted in his death. At no time was there any local sign of peritonitis. We attributed the gastric hemorrhage to cirrhosis of the liver.

In my next case the relationship between an acute diverticulitis and an intra-abdominal abscess is clearly proved:

S. D., aged forty-five years, had always enjoyed good health, He had never suffered from digestive disturbances, suggesting appendicitis, gallstone colic, or peritonitis. In August, 1902, while at dinner, he was suddenly seized with an attack of abdominal pain, nausea, and faintness, which necessitated his leaving the table and returning to his room. The attack soon passed off and he was able to join his friends later in the evening. The following night proved a restless one, as he had more or less constant pain in the lower portion of the abdomen, which prevented sleep, and at times was accompanied by nausea and general bodily weakness. The following day he continued to feel badly, but kept up and about for the reason

that he was a guest at a country house, and did not wish to inconvenience his host. Later in the day he went for a drive, and suffered acutely from the jolting of the vehicle. In the evening he was obliged to call a physician, who, after an examination, pronounced the case one of colitis. He returned to the city the following day, and as the symptoms continued, he remained in bed. During five days he continued to suffer with pain in the lower left quadrant of the abdomen, fever, and general malaise.

When first seen by me the temperature was 103°; pulse, 110; leukocytes, 17,000. There was marked rigidity of the left rectus muscle and a tender mass in the iliac fossa.

He was immediately removed to the Roosevelt Hospital, and, under ether anesthesia, an incision was made over the most prominent portion of the tumor. After dividing the tissues of the abdominal wall, a large abscess cavity was entered, which contained about 120 c.c. of foul pus, and an oblong, fecal concretion. On washing out the abscess cavity, a small ulceration was seen in the wall of the sigmoid, through which escaped a small amount of fecal matter. The cavity was packed with sterile gauze, the wound partly united, and a dressing applied.

After operation the temperature and pulse rapidly declined to the normal, the pain ceased, and the appetite returned. The discharge from the abscess cavity gradually diminished, until a cathartic was administered on the fourth or fifth day. This gave rise to a very abundant fecal discharge, which continued for several days. It gradually diminished after this period, and the sinus finally closed in about six weeks from the time of operation. He has since been in perfect health.

Three years later the following case was observed, which clearly demonstrated the relationship between an acute perforative diverticulitis of the sigmoid and a generalized fatal peritonitis:

A. W., aged fifty-four years, was admitted to the Roosevelt Hospital in August, 1905, suffering with the evidences of a rapidly developing general peritonitis. Four days before admission the patient had experienced severe pain in the abdomen, which was soon followed by nausea and vomiting. The pain at first was located in the region of the umbilicus, but later shifted to the lower abdomen, and finally became localized. In the beginning of the attack there was little or no fever, the chief complaint being the irritability of the stomach, which led to the belief on the part of his attendants that the patient was simply suffering from an acute attack of indigestion. Accordingly, a cathartic was administered, and other appropriate treatment advised. On the third day the symptoms became worse: there was more pain in the lower abdomen, a gradual rise in temperature, and a progressive increase in the pulse rate. The abdominal tenderness increased and a gradual distention appeared, with a renewal of the vomiting and a rapidly advancing prostration.

When admitted to the hospital his temperature was 103°; pulse, 128; leukocytes, 16,000. The abdomen was greatly distended, everywhere tender, and tympanitic to percussion. Muscular rigidity was well marked, as much on the left as on the right side. Examination of the heart and lungs was negative. The urine was loaded with albumin and granular and hyaline casts.

Acting on the belief that we had to do with a perforating appendicitis with spreading peritonitis, under ether anesthesia, an incision was made through the right rectus muscle. As soon as the peritoneum was opened there escaped a quantity of thin, foul-smelling pus. The intestines were deeply injected and matted together, and in places covered with a fibrinous exudate. The appendix was sought for and found to be intact and no more inflamed than the surrounding viscera. As the pus seemed to well up from the pelvis, the incision was enlarged, and the intestines drawn upward out of the cavity. At the bottom of this space we found an oval fecal concretion somewhat larger than a date seed; and, nearby, a deeply congested loop of the sigmoid, on the free border of which was the gangrenous remains of a small perforated diverticulum. The perforation was closed by Lembert sutures, the entire cavity washed out with normal salt solution, the wound partly united, and a cigarette drain carried down to the bottom of the pelvis.

The patient rallied well from the operation, but after forty-eight hours of improvement the vomiting returned, the abdomenn became more distended, the urine diminished in quantity, the temperature and pulse rose, and he became progressively weaker. All attempts to move the bowels were unavailing, and he died at the end of three days.

The last two cases prove conclusively the relationship between acute perforative diverticulitis of the sigmoid and a localized intra-abdominal abscess in one instance, and a spreading peritonitis in the other. They suggest also the probability that the concretion in each instance acted as a predisposing cause of the perforation.

That the condition is rare there can be no question, but that it is far more frequent than one would suppose from the scanty reference to it in medical and surgical literature I believe to be highly probable. While in four of my cases the relationship between a diverticulitis and the abscess is not proved, still the similarity in symptoms between them and the last two cases is so striking as to lead to the belief that they might well have had a similar origin, especially as it is difficult to account for their origin by any other theory.

THE ESTIMATION OF THE FUNCTIONAL POWER OF THE CARDIOVASCULAR APPARATUS.

A PRELIMINARY REPORT.

By Richard C. Cabot, M.D.,
and
R. B. Bruce, M.D.,
of Boston, Massachusetts.

Probably we are all fairly well satisfied with the ordinary methods for examining the heart and vessels in all cases in which, as we say, we *find something;* for example, in obvious valvular leaks, obstructions, and vascular degenerations. But there is a large group of cases in which we find nothing by auscultation and percussion, nor by the study of the palpable vessels and the examination of the peripheral parts and internal organs for evidence of passive congestion, even when these methods are supplemented by radioscopic examinations and blood-pressure measurements. "Heart negative" we often write; but we feel by no means sure that the heart is as sound as our examinations are negative.

Especially if we are interested, as no doubt we are, more in the question—"What can the heart do"—than in the question—"What anatomical lesions exist in it"—we need some supplement to the methods of examination above listed. In the differential diagnosis between cardiac neuroses and permanent organic damages of one or another description, between the nervous heart and the weakened heart, we are often in a quandary. Or, again, when we are not seriously in doubt about the diagnosis, but desire to know *how far* a patient's convalescence has advanced with respect to cardiac power, or *how far* a known lesion has weakened the cardiovascular apparatus, we sometimes find the ordinary methods of examination at fault. In such cases, following Rosenbach, we supplement them more or less by experiments. We say: "Work a bit, and see how much it tires you," or "Do you get out of breath when you go upstairs?" "How many pillows do you have to have at night?" "Do you have palpitation when you hurry?" These are very rough-and-ready methods, yet they sometimes yield us information of more value than our direct physical examination. In the attempt to render more accurate the data at which we aim by questions such as those just suggested, a number of procedures have recently been suggested by German writers. It is the purpose of this paper to describe some of these methods, and to report briefly our own experience with them.

I. The Effects of Changed Position. It has been noticed by Schapiro and others that the normal difference between the pulse

rate in a standing position and the lower pulse rate in recumbent position disappears when the heart is seriously weakened. In 100 cases we have tested this simple procedure—by counting the pulse first while the patient stands, and then while he lies flat: we find that the normal slowing of seven to fifteen beats per minute, which recumbency produces in healthy persons, is diminished or altogether lost in cases of uncompensated valvular disease, and when the heart is seriously weakened by any cause. We have not yet studied this test

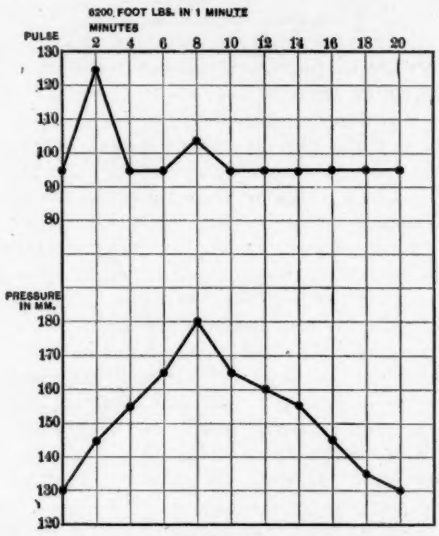


CHART I (which in our experiments represents the commonest type of normal reaction, or "*Erholung*" after exertion), shows a sudden rise in the pulse rate from 95 to 125 immediately following 6200 foot-pounds of work, accomplished in one minute by stair climbing. Four minutes after the performance of this work, when the pulse rate had fallen again to normal, the blood pressure had *risen* to 155, *or* 10 *mm. of mercury higher than it was when the pulse was most accelerated*. At the end of six minutes the pulse was still normal, but the blood pressure had risen to 165. At the end of eight minutes the blood pressure, continuing its rise, had reached 180 mm. After this a gradual fall in blood pressure occurred, the normal being reached only at the end of twenty minutes, although the pulse rate was normal in four minutes. Case 84,623. Normal. Aged twenty-four years.

extensively enough to know whether it would help us to recognize cases of *incipient* cardiac weakness not appreciable by the ordinary methods of examining the heart.

II. HERZ'S TEST.—Another procedure, suggested by Herz,[1] is called by him the Self-checking Test (*Selbsthemmungsprobe*). He counts the pulse over a period long enough to assure a reasonably constant rate per minute. He then has a patient sit down and very

[1] Deut. med. Woch., 1905, xxxi, 215.

slowly flex and extend the right forearm, putting all the while his full attention upon the movement, but endeavoring to avoid any contraction of the muscles. During this test the physician keeps his left hand supporting the patient's elbow, while his right hand, grasping the patient's wrist, directs the slow movements of flexion and extension, without, however, assisting or hindering them in any way.

Herz asserts that while in normal hearts this procedure exerts no influence upon the rate of the heart, a weakened heart is notably

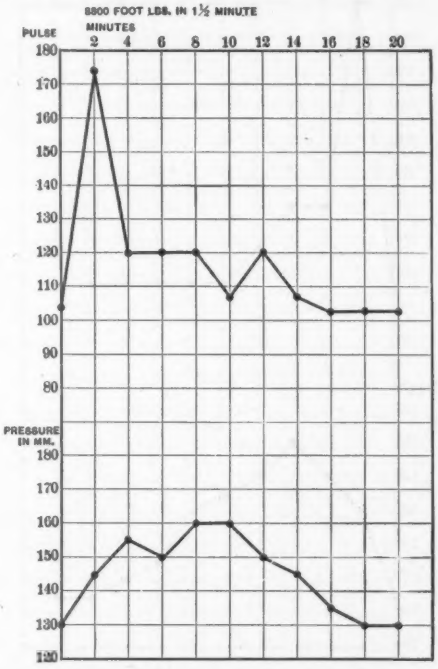


CHART II shows but slight variations from Chart I. In both of these cases the heart was young and apparently strong. Case 84,901. Normal. Aged nineteen years.

slowed. We have tested this method on 125 cases of miscellaneous affections, such as are seen in our out-patient clinic, and in a general way we have been able to confirm Herz's results. We have found that the great majority of cases in which the cardiovascular system shows no abnormality when examined by the ordinary methods, are also negative to Herz's test. A certain proportion of hearts which by other methods show evidence of weakness, react as Herz describes to the self-checking test; that is, the pulse slows down from 5 to 20 beats. In carrying out the test,

we have made it a rule that extension shall consume a full minute's time, and flexion also a minute. We are encouraged to follow this test further, although we have not as yet obtained any striking results with it.

III. LEVY'S TEST. Katzenstein's test[3] is based upon the well-known fact that if we increase the peripheral resistance opposed to

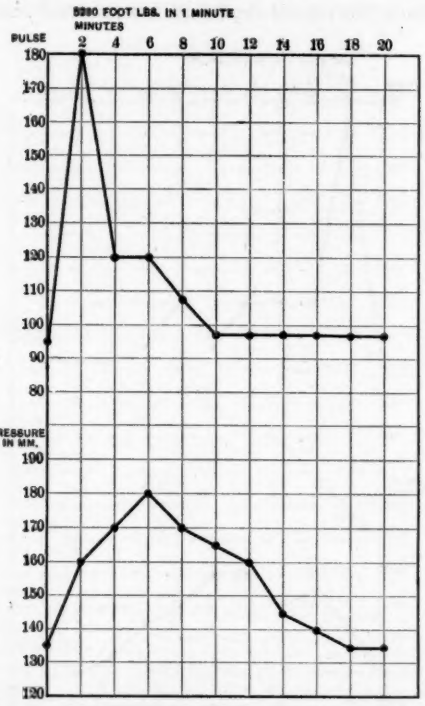


CHART III from a case of mitral stenosis, with perfect compensation, shows essentially normal conditions so far as this test is concerned. The rise in pulse rate, after 5280 foot-pounds of work performed in one minute, was more marked than in the normal heart, but the two charts are otherwise practically alike. Case 5354. Mitral stenosis. Aged twenty-one years.

the heart's action by compressing the abdominal aorta (in laboratory animals), a marked rise in blood pressure occurs. Anyone who is familiar with experiments on animals must have often seen the temporary resuscitation of a failing heart by compression of the abdominal aorta, and must also have noted that if the heart is quite exhausted, whether by hemorrhage or for other reasons, compression of the aorta is without its usual effect. In human beings

[3] Berl. klin. Woch., 1905, Nrs. 15 und 16.

Katzenstein imitates this familiar laboratory procedure by digitally compressing both femoral arteries at Poupart's ligament, and then noting the effects upon systolic blood pressure in the brachial artery. In normal persons this procedure is followed within two or three minutes by a rise of from 5 to 15 mm. of mercury in the systolic blood pressure. When the heart is hypertrophied (Levy[3] says) the

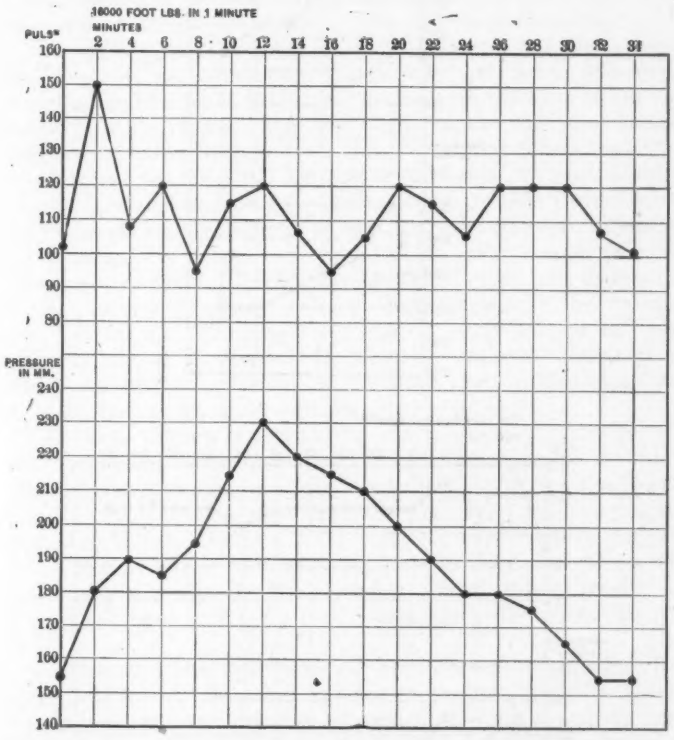
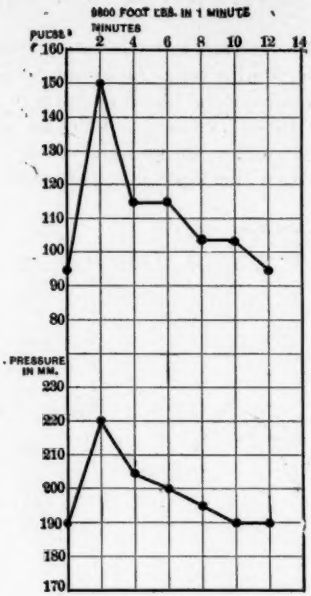
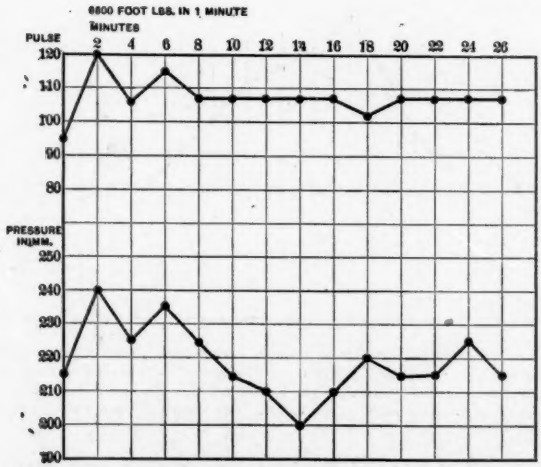


CHART IV shows the pulse and blood pressure curves from a case of weakened heart in a woman of forty-two. It will be noted that the "Erholung" is here *retarded*, so that the highest blood pressure is not reached until the end of ten minutes, while the return to normal occupies thirty-four minutes in all. Case 82,475. Myocarditis. Aged forty-two years.

rise is even more marked, while if the heart is weakened by any cause there may be little or no rise of blood pressure. Levy claims that no pain is produced by this procedure, but admits that it is useless in neurotic persons, since in them any such manipulation will suffice to raise blood pressure. We have made but few tests

[3] Zeit. f. klin. Med., 1906, lx, 1 und 2.





CHARTS V and VI illustrate the curves which we have found in a number of more seriously weakened hearts in older persons, with higher blood pressure than any of those shown in the previous charts. In these two patients a slight rise in blood pressure was simultaneous with the rise in pulse; thence it gradually declined to normal in Chart IV, and slightly below normal in Chart V. The characteristic increase of blood pressure after the pulse rate has returned to the normal level is absent in these two charts. Chart V. Case 84,478. Arteriosclerosis. Aged fifty years. Chart VI. Case 84,516. Hypertension. Nephritis? Aged sixty years.

of this procedure, as we have been unable to perform it without causing considerable pain, the effect of which would naturally be to raise blood pressure independent of any other cause.

IV. GRÄUPNER'S TEST. The test to which we have given the most attention is one of those elaborated by Gräupner[4] in several recent papers. Gräupner, who is a "Bad-Arzt" at Nauheim, found in the course of exercises prescribed as part of his treatment of cardiac cases that the reaction of weakened hearts after a measured amount of work differed distinctly from that of normal hearts. It is, of course, a familiar fact that the pulse rate and the systolic blood pressure rise after exertion, and that if exertion is sufficiently prolonged and arduous, both these figures may fall to or below the normal; but the phenomenon to which Gräupner has called special attention is quite different from this. Gräupner found that *after the pulse rate has risen and again fallen* to normal, as result of exertion, *the systolic blood pressure begins to rise,* reaches its maximum some minutes later than the pulse rate, and gradually falls thereafter to, or sometimes below, the normal. The phenomenon just described is that found by Gräupner in normal cases, and designated as the *"normal Erholung."* In weakened hearts, if the damage is but slight, the *"Erholung"* still occurs, but is delayed and perhaps diminished in degree. In seriously weakened hearts there may be no "Erholung" whatever, the blood pressure declining from the start, then gradually re-ascending to the normal.

The main outlines of Gräupner's contention may be easily verified by anyone. Run quickly up two flights of stairs, and then stop and count your pulse. After the immediate acceleration is past or during the slowing of the pulse following it, you will note that the heart beat and the strength of the pulse become markedly exaggerated. One feels the "thump-thump" of the heart against the ribs much more strongly after the pulse has almost or quite reached its normal rate than during the period when the pulse is most accelerated.

In performing this test, Gräupner used a weight-and-pulley ergometer, but in our clinic this was not convenient, hence we substituted a measured amount of stair-climbing. We reckoned the number of foot-pounds of work by the height ascended, computed in feet and multiplied by the number of pounds which the individual weighed. The amount of work in foot-pounds has, therefore, varied considerably, according to the weight of the individual, although the number of stairs climbed has usually been the same. As regards the phenomenon designated by Gräupner as the *"normal Erholung,"* we can verify his findings, and we likewise agree with him in the results of our experiments upon seriously weakened hearts. In some of the cases believed by us from ordinary examina-

[4] Collected in his monograph: Die Messung der Herzkraft, München, 1905, Otto Gmelin.

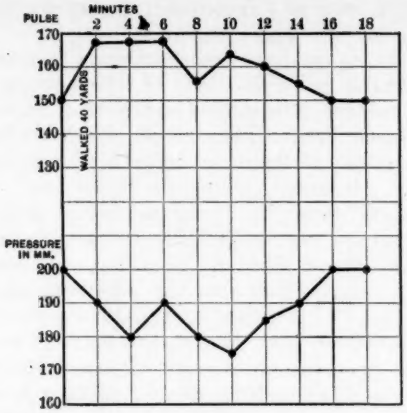


CHART VII shows the results obtained in a case of ruptured compensation, the patient being too ill to climb any stairs, markedly dropsical and cyanotic. Blood pressure *fell from the start* (simultaneously with a rise in pulse) and took eighteen minutes of perfect rest to bring it back to the (very high) point indicated at the beginning of the experiment. Myocardial weakness, cyanosis, etc. Aged forty-eight years.

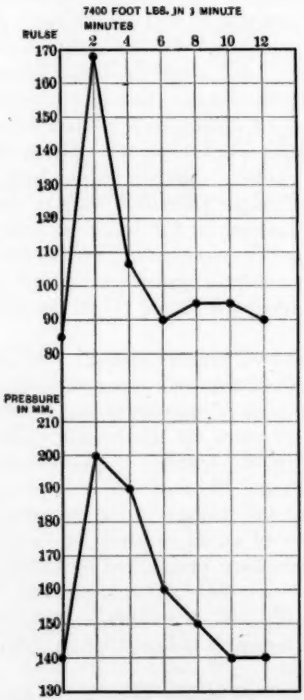


CHART VIII.—Case 84,318. Phthisis; "heart negative." Aged forty-five years.

tion of the heart to be normal, there was considerable variation from the ordinary curve of blood pressure after exertion. On the other hand, various cases of valvular disease with good compensation showed, as might have been expected, a normal curve. (See Chart II.)

The important question regarding this and the other tests above described is, of course, "Do they help us to recognize the presence or the degree of cardiac weakening not appreciable by the methods already in general use?" We do not feel prepared to decide this question

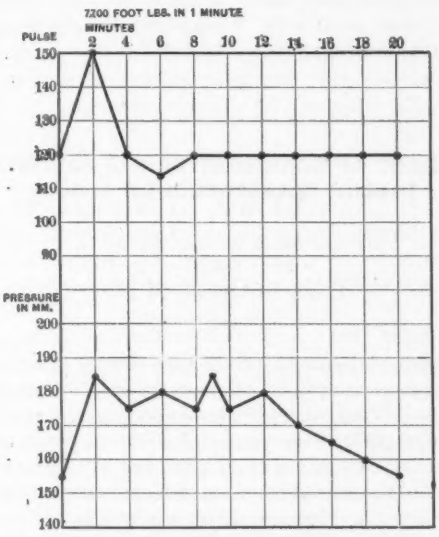


CHART IX.—Case 84,131. Palpitation. Nervousness. Myocarditis. Aged fifty-two years.

from the 75 experiments which we have been able to make in the four months during which we have been engaged in this work; but we have felt distinctly encouraged to continue the work, and in actual practice we find ourselves instinctively turning to Gräupner's test to verify our doubtful diagnoses of weakened heart, or to support us in the belief that the heart is normal when the patient has complained of subjective disturbances which might have been interpreted as evidence of passing congestion.

We suppose that the phenomenon just described depends primarily upon the amount of elasticity and contractile power in the arterial system; and, secondly, upon the ability of the heart to react upon the stimulus of increased peripheral resistance by beating more

strongly. In all our measurements the effect of age in diminishing arterial elasticity is strongly suggested; but we have not yet seen reason to believe that this is the only factor concerned.

SUMMARY AND CONCLUSIONS.

1. For diagnosis, prognosis, and treatment it is important to supplement the current methods of cardiac examination by others planned to measure the functional capacity of the cardiovascular apparatus.
2. Several such methods have recently been suggested by Germans.
3. Our experience with these methods, and especially with that of Gräupner, leads us to hope that ground has been gained in the direction of functional cardiac diagnosis.

THE TREATMENT OF ILLUMINATING GAS POISONING BY THE DIRECT TRANSFUSION OF BLOOD.

By George W. Crile, M.D.,
and
Carl Lenhart, M.D.,
of Cleveland, Ohio.

Occurrence. At least the main toxic factor in artificial illuminating (coal) gas poisoning is carbon monoxide. Carbon monoxide constitutes 6 to 10 per cent. of illuminating gas. It occurs in the so-called "water gas" to the extent of 30 to 40 per cent. It is the important toxic constituent of the "after damp" of mines, and of the gas from charcoal and coal stoves and from blast furnaces.

Mode of Action. Its action is purely that of asphyxia. It combines with hemoglobin, displacing the oxygen. Its affinity for hemoglobin is 300 times that of oxygen. The resulting compound is not perfectly stable, so that when oxygen is present in very great excess, carbonic oxidhemoglobin will be decomposed and oxyhemoglobin formed. Hence the rational treatment of patients by oxygen inhalation.

Haldane placed animals (mice) in oxygen under a pressure of two atmospheres, so that sufficient oxygen went into simple solution in the blood serum to support life independently of the hemoglobin. Sufficient carbon monoxide was present completely to saturate their hemoglobin. Under these conditions the mice remained normal as to symptoms, showing that the carbon monoxide has no direct toxic action. When the pressure was removed and the mice put out in the air they died with symptoms of asphyxia.

Haldane claims that in recovery carbon monoxide is given off from the lungs, as such, and is not destroyed or oxidized in the body.

SYMPTOMS. To summarize: there is stimulation of the central nervous system, followed by paralysis, the order being—brain, spinal cord, medulla. To detail:

1. There is cerebral excitement.

2. There is stimulation of the medulla: (*a*) Dilatation of the cutaneous vessels with flushing. The lips are pink. If the poisoning be very acute, there may be cyanosis, due to the fact that the venous blood does not yet contain much carbon monoxide. (*b*) The blood pressure rises, due to the stimulation of the vasomotor centre. There may be ecchymoses. (*c*) The heart is first slowed, due to vagus stimulation. (*d*) Respiration is dyspnœic. (*e*) There may be vertigo, vomiting, and mydriasis.

3. Paralysis of the medullary centres follows: (*a*) The blood pressure falls, due to vasomotor paralysis. (*b*) The heart rate is increased, due to vagus paralysis. (*c*) Paralysis of respiration (cause of death).

4. Following cerebral excitement there is unconsciousness, anesthesia, and coma.

5. There are often convulsions—from below up.

6. At death the hemoglobin is usually combined with the carbon monoxide to the extent of 60 to 80 per cent.

7. In dilute solutions the blood is pink and presents a characteristic spectrum.

8. Late symptoms and after-effect: these are quite lasting in man. They may be due in part to impurities in the gas. These late symptoms are prolonged unconsciousness or mental dulness, headache, nausea, spastic condition of the limbs, and epileptiform seizures. There may be loss of memory and mental derangement for months. Pneumonia may follow.

If the patients are breathing well when rescued, the blood is probably freed from carbon monoxide in about three hours. The danger from the condition of the blood itself is probably over in an hour, that is, if there is good respiration. But when the respiration is shallow and meager, this time is, of course, much extended. The late symptoms must be due, not to the blood condition directly (for this may be normal in a few hours), but to serious and more or less lasting injury to the nervous and other tissues. Hence, any measure tending to shorten the period during which the blood is impaired will tend to prevent the late symptoms due to tissue injury.

The above statements have been largely based upon Dr. Sollman's *Pharmacology* and Haldane's article in Hale White's *Pharmacology*.

Through the kindness of Drs. A. B. Kanavel, and H. M. Richter we have received by private communication the report of 16 cases of gas poisoning, occurring in the various services of Cook County Hospital, Chicago. Statistics based on these cases may render the matter more concrete and emphasize the need of treatment beyond that hitherto practised.

Number of cases 16.

Color. Mentioned 14 times. Cherry-red, 2; flushed, 1; cyanotic, 5; pale, 1; negative, 5.

Breathing. Dyspnœa, 15; apnœa, 1 (this case was associated with morphine poisoning).

Coma, 15; mentally clear, 1.

Pupils react to light, 7 out of 11 times tested; 4 did not.

Musculature. 3 had general tetaniform convulsions; 1, muscular tremor; 2, general rigidity; 2, stiff jaws.

Pulse, ran from 96 to 200. 11 cases had as their highest pulse rate 120 to 160.

Reflexes (knee-jerks). Mentioned 12 times. Present 9 times, exaggerated once, absent twice.

Temperature. Classified according to highest reached: 98° to 99°, 1; 101° to 102°, 1; 102° to 103°, 3; 103° to 104°, 1; 104° to 105°, 1; 105° to 106°, 2; 106° to 107°, 3; 107° to 108°, 2; 109.2°, 1 case.

TREATMENT. All received the usual stimulant drugs; 10 received oxygen inhalations; 4 were bled 10, 6, 4, and 8 ounces; 5 received intravenous saline injections; and all 16 cases died.

(*a*) Artificial respiration. It is needless to give reasons for its use.

(*b*) Fresh air.

(*c*) Oxygen is certainly indicated, not to oxidize the carbon monoxide, but by being in great excess gradually to displace it.

(*d*) Heat. Many persons have collapsed on being taken into the cold air, hence, it would seem better to institute treatment in a warm room.

(*e*) Patients have often died from exertion; for example, from violent endeavor to escape from a mine. There is probably acute dilatation of the heart in these cases.

(*f*) Stimulants such as camphor, caffeine, digitalis, strychnine, etc.

(*g*) Venesection. This method is rational when combined with the injection of salt solution or blood. As to its use alone, it is condemned by most of the older writers on the ground that it further depletes a patient already in a low condition. On the other hand, Halstead reported 2 cases in which he thought it did good. Reviewing the literature, Halstead thought that no case had been saved by transfusion when venesection had failed. This was in 1884.

(*h*) Transfusion of defibrinated blood by the older methods, together with venesection. This is mainly of historical interest. The theory was that venesection rid the body of some of the poison and the transfusion would replace the lost hemoglobin with fresh hemoglobin. The basis of this procedure was the experimental work of Kühne in the 60's of the last century. In a monograph by Willy Sachs,[1] his work is summarized as follows:

[1] Die Kohlenoxide Vergiftung, 1900.

1. Animals poisoned until eye reflex is absent recover spontaneously, provided respiration is not reduced below 2 per minute.

2. If respiration be reduced to 1 a minute, they do not recover unaided. If bled smartly they usually recover.

3. If respiration stop for a few minutes, they do not recover even though the heart is beating well, and even if they be bled and given artificial respiration.

4. Even after respiration has stopped several minutes (1 case seven minutes) when there is no peripheral pulse, no heart beat detected through the chest wall, and often with the animal in convulsions, transfusion of blood will bring back life.

There is this criticism to be offered concerning Kühne's experiments. He groups his cases largely on a basis of the rate of respiration. We have found that this is very irregular, so much so that one could never definitely say that the respiration was 2 or 1 a minute. In fact it is difficult to say when respiration has finally stopped. A large majority of the dogs stopped breathing for two or even five minutes and then began again with a fairly good quality of respiration. So we think that many of Kühne's good results were due to the fact that he began his measures during this first interval of cessation of respiration; and his dogs were not nearly so dead as he thought.

On the basis of these experiments, clinical cases of gas poisoning were transfused. This was in the 70's and 80's. Favorable cases were reported by Utuhart, Badt, Bouveret, Lühe, Rüdinger, Kahler, and Leyden. To mention a few instances, Von Heuter (1870) had a patient who was unconscious and upon whom artificial respiration had to be maintained. 500 c.c. of defibrinated blood were transfused. The patient regained consciousness in a few hours and recovered.

Leyden had a patient found in coma at 5 A.M. Venesection and artificial respiration brought no improvement. At 11.15 A.M. he had no corneal reflex; respiration was slow, irregular, and shallow; pulse bad. At 1 P.M. 250 c.c. of defibrinated human blood was transfused. At 6 P.M. he turned over in bed. At 4 A.M. he wakened, drank milk, and went on to complete recovery.

Friedberg, while he reported 3 unfavorable cases, still favored transfusion. He thought its failure due either to insufficient and poor blood, or to great injury to the nutrition of the respiratory and circulatory systems.

Albert mentions 2 cases. One had re-acted to none of the usual stimulants; heart was barely perceptible. Was transfused, recovered and could stand the next day. Another case of seemingly the same degree of intoxication was not transfused. This patient was three days unconscious. He finally lived but had the late symptoms, nervous trouble, for a month. Albert, therefore, favored transfusion.

Opposed to these favorable views were such men as Hunter and von Bergman, who thought that the danger of thrombosis and

embolism outweighed any advantage that transfusion might have. Among pharmacologists, Kobert favored and Kunkle opposed transfusion on the same grounds.

(*i*) Refusion of blood. Halstead, in 1884, recorded a case treated by this method. Patient was comatose, respiration 28, shallow, pulse, 96, small, easily compressible. There was general rigidity. 512 c.c. of blood was withdrawn from the right radial artery, defibrinated and strained. 288 c.c. was reinfused centripetally into the artery. The patient made a good recovery.

(*j*) Saline intravenous infusion. In the 80's the transfusion of blood was forsaken and everyone turned to the new physiological saline solution. We have found the following recorded:

I. Jersey[2] reported a patient in collapse for twenty-four hours. Was bled 8 ounces and given 11 ounces of salt solution intravenously. Patient recovered.

II. Wilkie[3] reported 2 cases.

1. Bled 13 ounces; solt solution 13 ounces; recovery.

2. Bled 6 ounces; salt solution 13 ounces; death. Marked temporary improvement.

III. Schruber reports a patient unconscious and in convulsions on the second day. Eleven and one-half hours after having been given saline infusion he began to speak and finally recovered.

IV. Von Gordon reports 3 cases:

1. Patient unconscious, slow stertorous breathing, pulse weak and irregular, 72, reflexes lost. Bled 300 c.c.; saline 400 c.c.; recovered.

2. Patient unconscious, respiration irregular, pulse dicrotic, irregular, 120. Convulsions. Bled 300 c.c.; salt solution 300 c.c.; recovered.

3. Patient unconscious, convulsions, dyspnœa. Bled 165 c.c.; salt solution 300 c.c.; recovered.

V, VI, VII, and VIII. From Cook County Hospital cases, all terminated fatally.

Our review shows:

(*a*) The older experimental work seems faulty and insufficient.

(*b*) The clinical evidence is variable but, on the whole, leads one to have hope that the newer method of transfusion of blood will be of considerable value in these cases.

Our own research was instituted to test the value of the various therapeutic measures suggested, especially blood transfusion. Dogs were used. Ether was the anesthetic. Various forms of apparatus were used. The last one used was a large, air-tight, iron tube, into which gas and air entered through water bottles, by the bubbling of which one could make a rough guess as to the amount entering. No attempt was made to determine the exact proportion of gas in

[2] Cited by Bull. New York Med. Record, 1884.

[3] Ibid.

the mixture. It was decided, owing to the varying susceptibility of the animals, that the best basis for comparison of therapeutic measures would not be the percentage of gas, its quantity, or its time of action (that is within narrow limits), but rather the exact condition of the animal as determined according to ordinary clinical means, and especially by a manometric tracing of the blood pressure. Consequently, the carotid artery was attached to a manometer with a style writing on a revolving drum, in the usual way. A tracheal cannula was inserted and connected to a T-tube. The two branches of the T-tube were connected to valves made of fingers of rubber gloves, set in small flasks. One valve opened with inspiration, the other with expiration. The valves were connected respectively with the gas tank and the outside air, so that the dog inspired the gas mixture and expired into the outside air. The dogs were thus poisoned, and when the blood pressure reached a certain low point the various therapeutic measures were instituted and their results compared.

It would require too much time to give the history of individual experiments. A few statistics of the results may be of interest.

In all cases respiration had stopped. In the 16 cases recorded the heart had stopped in 8 cases before any measures of resuscitation were taken. Immediately the heart stopped, however, these measures had to be begun. Resuscitation was never accomplished after the heart stopped for any length of time. In 6 cases the heart had almost stopped, with a blood pressure varying from 8 to 20, with an average a little under 14 mm.—certainly a low blood pressure. In 2 cases the blood pressure was 54 and 44 mm. One was saved by transfusion, the other died notwithstanding the giving of saline.

(*a*) Animals treated by bleeding, manipulation of the heart, and artificial respiration. One experiment. Died.

(*b*) Animals treated by bleeding, intravenous saline, manipulation of the heart, and artificial respiration. Three experiments; 3 died.

(*c*) Animals simply treated by manipulation of heart and artificial respiration. Two experiments; 2 died.

(*d*) Animals treated by blood transfusion, bleeding, manipulation of the heart, and artificial respiration. Ten experiments; 7 lived, 3 died.

Reduced to the low degree of blood pressure, 7 out of 10 were rescued by transfusion of blood; 6 other dogs treated by the various other methods all died.

Of cases in which the heart stopped:

1. Blood transfusion saved 3 out of 6.
2. Intravenous saline. None saved; 1 died.
3. Simple manipulation. None saved; 2 died.

Of cases in which the heart almost stopped:

1. Blood transfusion saved 4; 1 died.
2. Intravenous saline. None saved; 2 died.

These experiments include only those done while taking a blood-pressure record on the manometer, so that the exact condition of the dog could be constantly watched.

A large number of experiments have been discarded, in which no drum record was taken, because it was found that if the exact status of the dog was judged clinically, that is, by pulse rate, stethoscope, etc., the results were so variable and so far from following any rule, so different from the above results, that one was forced to the conclusion that the starting point for initiating the various therapeutic measures was not being made reasonably the same. Hence, the conclusions could not be exact enough to be of value. Instead of an experiment with exact limitations, we were simply reproducing clinical cases, as seen in the hospital.

By recoveries we mean cases in which the blood pressure comes back approximately to the point where it started and remains fairly constant for an hour or so, and in which the respiration becomes spontaneous and of good quality again and the reflexes reappear. Actual recoveries were not done because of the difficulty of maintaining asepsis with our present means, especially while taking blood pressure records with a cannula in the carotid artery.

CONCLUSIONS. 1. Blood transfusion seems to be of greater therapeutic worth than the other measures considered.

2. For the animal to recover, it is necessary to begin transfusing immediately the heart stops beating. It is not efficacious after the heart stops finally, as, for example, is adrenalin in chloroform death.

THE EXAMINATION OF THE FECES FOR OCCULT BLOOD, WITH SPECIAL REFERENCE TO THE VALUE OF THE BENZIDIN TEST.

BY EDWARD H. GOODMAN, M.D.,
OF PHILADELPHIA.

(From the private laboratory of Dr. John H. Musser, Philadelphia.)

SINCE Boas,[1] in 1903, directed the attention of the medical world to the significance of small hemorrhages (unrecognizable macroscopically and called by him "occult") from the gastro-intestinal tract, the study of the feces from this viewpoint has become one of the most important of the routine clinical laboratory examinations. Since time immemorial, until comparatively recent years, the finding of blood arising from the gastro-intestinal tract was a very crude procedure and limited to but one means, the sense of vision. Either the hemorrhage must have been high up and have shown itself from the mouth as bright red blood, or as so-called "coffee-ground

[1] Deut. med. Woch., 1903, No. 47.

vomit;" it must have been low down (hemorrhoids, ulcers, etc.), when it would make its appearance in the feces as easily recognizable streaking; or the hemorrhage must have been intestinal, and comparatively large, in order to lend the feces the classical "tarry" appearance. If this macroscopic examination sought substantiation in the microscope, we fear the observers were often doomed to grievous disappointment, for inasmuch as most of the red blood cells are rapidly destroyed in the upper portion of the intestinal tract, their appearance microscopically in the feces must have been one of great infrequency and rarity.

We now know that only exceptionally has the color of the feces any relation to the presence or absence of blood. We have all seen the typical fatty stool, of very light color and offensive odor, yielding a beautiful chemical test for blood, whereas, with less accurate means at their disposal the older observers would have been disposed to regard the stool negatively as regards blood. It is this hidden, insidious bleeding which, since Boas' article, has received such attention, that we must now regard and not direct all our thoughts toward the macroscopic bleeding. While the latter is, of course, important, the former is much more so. It is well known that a large profuse hemorrhage is often preceded by a very small, macroscopically not recognizable, bleeding, hence, if this can be detected, and properly treated, a large hemorrhage may often be averted. On the other hand, when a routine examination of the feces is not made regularly for each patient, the macroscopic appearance of the stool may often lead to a more minute examination. If, for example, the case is one of colica mucosa, the macroscopic examination discloses ribbon-like pieces and meshes of mucus, which, if examined microscopically, are seen to be covered with red blood cells. In this case, and in some cases of intestinal carcinoma, the microscopic examination is seen to be more important than a routine blood test, for it leads to a diagnosis, whereas, the occult blood test at the best is but an aid in determining the nature of the morbid process. So, because we have a reasonably simple and exact test, we must remember not to put all our reliance on it alone, but must call to our assistance simpler methods, which, in this era of scientific research, with its accompanying accurate methods of examination, reliable instruments of precision, and unimpeachable chemical tests, we are too likely to overlook.

The methods employed today for the detection of macroscopically invisible blood are based on a test of a single chemical constituent of blood, namely, blood coloring matter, or one of its near substitution products. It is unnecessary to explain each test in detail, as descriptions may be found in the various text-books, and in a very careful and instructive monograph by Schumm,[2] from

[2] Die Untersuchung der Feces auf Blut, Jena, 1906.

whom I have derived much benefit in preparing this paper. It will suffice to mention only the tests now used:

The *Teichmann Hämin test* (rarely employed).

The *Nencki-Koberts acetonhämin test*, in which the diagnosis is made by a microscopic examination of the hämin crystals. The feces are first freed from fat by means of alcohol followed by ether, and after adding a drop of concentrated hydrochloric acid, the stool is ground up with aceton. The feces are now boiled and filtered hot into a watch crystal, a few drops only being collected on a slide. On rapid evaporation, the hämin crystals are seen on the latter as "extremely characteristic, long, curved, hair-like crystals" (Nencki), while on slower evaporation in the watch glass they are thicker. Schumm has tried this test, but does not advise it for clinical purposes.

The Spectroscopic Examination. For this purpose the acetic acid-ether extract obtained while doing Weber's test may be used, or the suggestion of Schmilinsky[3] may be followed. Schmilinsky recommends the conversion of hematin into hematoporphyrin by grinding up a small portion of feces with water and adding from a few drops to a few cubic centimeters of concentrated sulphuric acid. By using a vessel with flat sides, the characteristic absorption lines may be seen. He recommends in case of negative findings the use of the guaiac test, as being more sensitive. If the characteristic lines are present there can be no doubt about the presence of blood, as, to our knowledge, no substance but blood gives a similar spectrum. I have had very little experience with the use of the spectroscope in looking for occult blood and can give no advice based on personal observation.

The tests that are generally employed at the present time are the guaiac (Weber's) and the aloin (Rossel's) tests.

Weber's Test. Weber's own directions are as follows: A large portion of feces is ground up with water, to which one-third its volume of glacial acetic acid has been added, and this mixture is extracted with ether by shaking. After standing a short time, a few cubic centimeters of the acid-ether extract is poured off and ten drops of the tincture of guaiac and thirty drops of turpentine are added. In the presence of blood the mixture becomes blue violet, whereas a reddish-brown color with a shade in green is noted if blood be absent. The reaction becomes more pronounced if the blue color is extracted with chloroform, after first adding a little water to the acetic-acid-ether extract.

Weber speaks of some sources of error which are mentioned by Schumm, and the latter observer has found that frequently in following Weber's method an emulsion has formed which was often hard to remove, but he succeeded eventually with alcohol. He found it

[3] Münch. med. Woch., 1903, 2145.

necessary sometimes to add alcohol, then ether, and then more alcohol. Boas has made the objection that alcohol sometimes produces the blue color, but Schumm, in thousands of examinations, says he has never seen alcohol alone give this color.

Schmilinsky says that ozonized turpentine gives the characteristic color if it has stood in direct sunlight, which observation Schumm substantiates, but says the turpentine can be again brought to normal condition if put in a shady place. He recommends putting the turpentine in large open vessels, and letting it remain in a semi-dark cellar for weeks.

Rossel[4] was the first to recommend the removal of fat by drying the stool and then extracting with ether in a Soxhlet apparatus; Schumm very properly takes exception to this, as being a too complicated procedure for ordinary clinical purposes. v. Koziczkowsky[5] modifies Rossel's suggestion and shakes the stool with ether, or grinds it up with ether, pours off the ether, mixes the feces with glacial acetic acid, extracts with ether by shaking, and tests the etheral extract. This method also calls forth an objection from Schumm, who offers a modification of Weber's test for which he claims many advantages.

Schumm's Modification of Weber's Test. If the stool is thick, he takes 4 grams of feces (about the size of a small walnut) and grinds it up with equal parts of alcohol and ether, 30 c.c., in a glazed porcelain mortar. He filters through a pure open filter, covers the residue with alcohol and ether, and mixes by gently stirring with a glass rod. This is allowed to filter, covered with ether, and gently stirred. After the ether has filtered through he again washes with ether and again filters. In this way soluble coloring matter, neutral fat, fatty acids, and water are removed. The washing is complete when the filtrate is only slightly colored, and, if desired, the filtrate can be used for hemin crystals; otherwise, it is disregarded. The residue remaining on the filter, which, besides food-rests, contains soaps and coloring matter not soluble in neutral alcohol-ether, is covered (on the filter) with 4 c.c. of glacial acetic acid and mixed by gently and thoroughly stirring. After the greater portion has filtered, 4 c.c. of glacial acetic acid is poured on and stirred with the fecal residue. After most of the acid has been filtered, it is poured back on the filter and again mixed carefully. In order to avoid the annoying fumes of the acid, he advises covering the funnel with a watch glass.

By this method blood coloring matter is set free and the organic katalizers (oxydizing ferments) are destroyed. In the absence of blood coloring matter the filtrate is rather deeply colored. Several cubic centimeters of the glacial acetic acid filtrate is diluted with its volume of ether, half the volume of distilled water is added, and the whole taken. If the fluids do not separate add some alcohol, ether, or water.

[4] Deut. Arch. f. klin. Med., 1903, lxxvi, 505.
[5] Deut. med. Woch., 1904, xxxiii, 1198.

The ethereal solution is separated and again shaken with a small amount of water. This ethereal solution is to be tested in absolutely clean test tubes with guaiac tincture and turpentine. (Schumm warns against using test tubes already used for sugar tests; if no others are available, however, they may be used if washed with acetic acid and alcohol.) In the presence of hematin the color is more or less blue, violet, reddish-violet, as well as greenish-blue. Schumm claims that the Weber test, even in the presence of not inconsiderable amounts of blood, sometimes gives only a rapidly disappearing violet coloring, whereas, in the above modification, the color is slower in appearing, but is also more lasting. For thin stools the method is the same, only larger amounts must be used. Schumm recognizes the fact that in his modification a certain amount of blood is lost, but claims the quantity is inconsiderable and may be disregarded; as a control of his modifications he recommends the use of the spectroscope, which gives, to a certain extent, the quantity of blood present.

The question of just what shade shall be regarded as indicating the presence of blood seems to have been the source of much confusion in the reports of various authors who have studied the Weber test. Schmilinsky says not only the *blue* color is positive, but also the various other related colors. He does not consider the green color absolutely indicative of blood, as the ether sometimes takes up this color from the feces, and this interferes with the test, but if the green color appears it should be regarded as suspicious, and the test should be made more exactly with less ether in order to get a concentrated hematin extract; the test should be repeated on the following day, and the spectroscope should be used as a control. Schloss[6] found, as did Hartmann, whom he quotes, that only the blue-violet color indicates blood, and that all other shades arise from some coloring matter in the feces, and in this view he is supported by Schumm. The latter gives the following colors as being positive for his modification: ½ minute, green; 1 minute, blue green; 2 minutes, violet.

The Aloin Test of Rossel. Rossel makes a solution of Barbadoes aloin by putting as much aloin as will go on a knife point in 3 to 5 c.c. of 60 to 70 per cent. alcohol. He extracts the fat from the feces and makes a glacial acetic acid-ether extract, adding to this 20 to 30 drops of old turpentine and 10 to 15 drops of the aloin solution. In the presence of blood there is a beautiful cherry-red color appearing in from five to ten minutes; whereas, in the absence of hematin, the color first shows itself in from one to two hours, and remains. He advises making a fresh aloin solution each time before using, and claims the test is as sensitive as the guaiac test, for, after making experiments on himself, marking off his feces with charcoal, he found a positive reaction with 10 c.c. of blood.

[6] Arch. f. Verd.-krankh., 1904, x, 267.

Benzidin Test of O and R. Adler.[7] As given in the original paper of these authors the test was found to be inapplicable for clinical purposes, and two important modifications have been proposed.

The first is from Schumm, who cleanses the stool first with alcohol and ether, as in Weber's test, and extracts with glacial acetic acid. The extract is washed with 1 to 2 c.c. of water, the acid-ether extract is then mixed with 2 c.c. of benzidin solution and H_2O_2 added. The second modification, which I have used exclusively in my studies, is that practised by Schlesinger and Holst,[8] with but a few changes. The following is the method of Schlesinger and Holst:

1. A concentrated solution of benzidin is made by using as much benzidin as will go on the end of a knife in about 2 c.c. of glacial acetic acid. (For several tests, correspondingly more.) The benzidin is readily soluble, and the mixture should be shaken a few times.

2. A small piece of feces about the size of a pea is taken up on a glass rod and suspended by stirring in a test tube one-fifth full of water; the test tube is closed with cotton and the feces are boiled.

3. Ten to 12 drops of the benzidin solution are poured into a test tube and 2.5 to 3 c.c. H_2O_2 (3 per cent.) added.

4. To this are added 1 to 3 drops of the boiled feces, after mixing by slightly shaking.

In the presence of blood the color becomes green, blue green, or blue, the blue being more pronounced if more blood is present. Slight amounts show a reaction in one-quarter to one-half minute, and very small amounts always within two minutes. After five to fifteen minutes the color becomes a dirty dark red violet and remains so. Negative tests show no change even after standing twenty-four hours.

Sensitiveness of the Guaiac, Aloin, and Benzidin Tests. The guaiac and the aloin tests have been found to be about equal in sensitiveness and both respond to blood in the dilution of 1 to 25,000; whereas the benzidin test is positive in a dilution of 1 to 200,000 (Schumm and Westphal).

Sources of Error in the Various Tests. In making any test the source of error must be kept in mind and removed as far as possible before a test can be considered as having any importance.

Guaiac Test. Rossel says the main disturbing agent is iron, and the importance of discontinuing the use of iron while the feces are being examined for occult blood has been discussed by Adler, Schumm, and others.

Every worker on the subject of occult blood has come to the conclusion that meat in the ordinary diet very often gives the guaiac test. Schmilinsky, in 1903, recommended a diet of milk, with coffee or tea, milk soups, sugar, butter, bread, rice, sago, farina

[7] Ztschr. f. phys. Chem., 1904, xli, 59.

[8] Deut. med. Woch., 1906, xxxvi, 1444.

and oatmeal, eggs, etc. He examines the stools on the third day. v. Koziczkowsky uses a similar dietary, but advises against the use of much fat and vegetable (chlorophyll often disturbs), and he marks off the stool with charcoal in preference to carmine, which he thinks interferes with the test.

Rossel advises the use of freshly made tincture of guaiac, or, if an old tincture is used, this should be tested with a weak blood solution. Schumm also advises fresh guaiac. I have used old guaiac and found it satisfactory for a period extending over some weeks. The turpentine, of course, should be old and should not have stood in sunlight, and before using as a testing solution its reliability and maturity should be first tried on a bloody stool or on a blood mixture.

Aloin Test. Rossel does not lay much stress on disturbing factors, except fat. A fresh solution of aloin should always be made, as in time it assumes the red color seen with blood. There seems to be a difference of opinion between observers as to the value of this test. Rossel, Boas, and v. Koziczkowsky prefer it to the guaiac test, while Schloss seems to think there is nothing to choose between them. Schumm agrees with him and supports him in his view that both should be used as controls.

Benzidin Test. Owing to its simplicity, this test will doubtless find its way into every laboratory, but in using it several precautions must be borne in mind.

1. The benzidin must be pure, and only Merck's benzidin puriss. should be used. This was found by Schumm and Westphal to be ten times as active as the benzidin puriss. of other firms.

2. The same authors claim that a positive reaction depends on the relative amount of the individual agents. An excess of H_2O_2 can cause a disappearance of the green color, consequently, if too much H_2O_2 is used in making the test no green color appears. Therefore, the H_2O_2 should not be stronger than 3 per cent., and but 2 c.c. should be used.

3. The following substances were found by various authors to give a positive reaction with benzidin: Oxydizing ferments, animal as as well as vegetable (readily destroyed by boiling); iron salts, pus, saliva, nasal secretion, bowel detritus, and mucus give a more or less positive reaction; potassium iodide, pure animal charcoal, metallic iron, platinum, and copper in all forms. (One should be careful of the test tubes used for sugar reactions.[9])

Schlesinger and Holst made a comparative study of the aloin, guaiac, and benzidin tests, in the endeavor to find a simple test for occult blood in the feces. They used three modifications of the guaiac test, including Schumm's improvement, and in feces from persons on ordinary meat diet all three tests, the aloin, guaiac, and

[9] Ztschr. f. phys. Chem., 1905, xlvi, 510.

benzidin were found to be positive. On small amounts of meat (test diet) the aloin and guaiac tests were negative, excepting Schumm's modification of the latter, which was positive, as was also the benzidin test. In meat-free diet, all tests by all methods were negative.

In using the benzidin test as modified by Schumm, they did not observe a negative reaction. In two long meat-free experimental series made on themselves, the guaiac and aloin tests were negative forty-two to sixty-five hours after the last stool from a meat diet, while the benzidin test (Schumm) was positive on the eighth, even on the tenth day. As it is impossible to continue a meat-free diet for ten days, the Schumm benzidin test is hardly to be recommended. Schumm himself said the test was too "subtile," and hesitated about advising its use, as did Boas.

As regards the guaiac test, Schlesinger and Holst both consider Schumm's modification a refinement and, if made according to his directions, it is much more sensitive than aloin, whereas, if done in the ordinary way, aloin is the more sensitive, as the guaiac test is often masked by an olive-green color. When many feces are to be examined, Schumm's method takes up too much time to be of much service as a routine test. Schlesinger and Holst recommend the benzidin test in the above described method for the following reasons:

1. It is simpler than any other method.
2. It is sharper than the aloin and guaiac tests, but is, nevertheless, applicable for practical use, which the guaiac test of Schumm is not.
3. By boiling, all disturbing factors, such as ferments, are destroyed.
4. We have a control of the reagents, making the test more sure.

Schlesinger and Holst made experiments with weighed portions of blood-free stools and bloody stools, and found that 0.25 gram of tarry stools plus 5 grams of blood-free stools gave a positive aloin and guaiac test. With 0.05 gram + 4 grams the aloin and guaiac tests were negative, while 0.05 gram tarry stools + 20 grams blood-free stools gave the benzidin reaction (green). They made observations on themselves, taking meat-free diet until the stools remained negative for blood for some days, then, at luncheon, with a cup of tea and sugar, they took a weighed portion of fresh blood, 0.5 gram, obtained by pricking their fingers. On the third day, in one instance, there was a positive benzidin reaction, while, with Schumm's modification of the Weber test there was only a green color, which Schumm regards as negative. The examination of the other stool was negative, perhaps due to a disturbance of the intestinal function evidenced by fermentation and subjective symptoms. It is thus seen that ten drops of blood are sufficient to give a positive benzidin reaction, while, in comparison, Rossel's test first shows a reaction with 10 c.c. blood (after 5 c.c. generally nega-

tive), and Schumm's modification of the guaiac test a positive result with 2 c.c.

The afore-mentioned authors, together with Oettinger,[10] and Oettinger and Girault,[11] have used the test with various degrees of satisfaction; the rosy accounts of its partisans were so encouraging aging that I was led to make a comparative study of a number of feces, in order to learn what might be expected from this much vaunted and much disputed test.

I found, in the first place, that taking a piece of feces the size of a pea and mixing it in a test tube with water (as advised by Schlesinger and Holst) was not practicable; moreover, it did not seem reasonable to examine such an isolated portion of feces. If the blood is not equally distributed throughout the stool, the chances of selecting a portion of feces containing blood becomes questionable. I preferred to grind the feces with distilled water and to examine a boiled portion of this.[12]

According to Schumm, the first advantage claimed by Schlesinger and Holst, namely, simplicity, is sacrificed by boiling. The time necessary to bring the feces to a boil is insignificant, at the most fifteen to thirty seconds, and I fail to see how this manipulation interferes with the simplicity of the method. Schumm further contends that, while boiling destroys the oxydizing ferments it does not affect the inorganic substances, such as potassium iodide and animal charcoal, which substances react to the benzidin test. So, in common with v. Koziczkowsky and Schlesinger and Holst, he recommends the use of vegetable charcoal to mark off the feces. Schlesinger and Holst,[13] in a reply to this article, accept Schumm's suggestion about grinding up feces in a mortar, instead of selecting an isolated piece, and mention that in using the benzidin test potassium iodide and animal charcoal are always previously eliminated.

In the present series of observations no attempt was made to eliminate meat from the diet, as the primary object was to compare the relative values of the three tests, and not to make a clinical study of diseases from the viewpoint of the presence or absence of occult bleeding. The tests used in this series were the guaiac, the aloin, and the benzidin tests. For the first two tests a portion of the feces was first ground up with distilled water in a glass mortar, a portion of this put into a separating funnel and shaken with ether to extract the fat. By using repeated small portions of ether I rarely met with any difficulty from emulsion formations. Did this occur, the addition of more ether invariably caused the complete separation. The ether and feces were poured into a large, wide-necked test tube, and the ether then poured into a bottle for

[10] Jour. des. pratic., 1906, 451. [11] La semaine méd., 1906, 325.

[12] Since beginning this research, Schumm, Münch. med. Woch., 1907, has published a paper in which he advises the same procedure.

[13] Münch. med. Woch., 1907, 460.

waste ether, to be redistilled later.[14] The remaining fat-free feces was shaken with equal parts of glacial acetic acid; then 10 c.c. ether was added and the mixture again shaken, and allowed to stand until the ethereal extracted had separated from the fecal residue. The acetic acid ether extract is used for the aloin and the guaiac tests.

A few cubic centimeters of the extract are poured into one test tube and a few cubic centimeters of ethereal extract of guaiac are added, then an equal quantity of H_2O_2 (3 per cent.), and the whole shaken gently. Only the blue color of the ether was regarded as indicating blood, other colors being considered as negative.

Into another test tube are poured a few cubic centimeters of the glacial acetic acid-ether extract and 2 to 3 c.c. of the aloin solution is added. (This solution must be made fresh each time by dissolving as much aloin as will go on the end of a knife in about one-third of a test tube of 70 per cent. alcohol.) To this 2 to 3 c.c. of ozonized oil of turpentine are added and the test tube gently inverted several times. In the presence of blood the lower layer of aloin becomes a cherry-red color, but if the color does not appear in from five to fifteen minutes it should be considered as a negative test, as often by that time the aloin itself gradually assumes the same cherry-red color. The above two methods are those used by Steele and Butt,[15] and have been found to be most satisfactory.

Benzidin Test. For this purpose I recommend the following procedure: A small portion of the feces solution, obtained by grinding up the feces with water, is poured into a test tube and boiled. While this is cooling, a concentrated solution of benzidin is made by dissolving as much benzidin as is contained in a very small spoon spatula in about 3 to 5 c.c. of glacial acetic acid. A few drops (1 c.c.) are poured into a test tube and about 3 to 10 drops of this boiled feces solution further diluted with equal parts of water, are added and the two shaken. To this are now added 1 to 3 c.c. H_2O_2 (3 per cent.) and shaken, when, in the presence of blood, a deep, dirty green or a beautiful deep blue color appears, changing in the course of time to a peculiar dusty violet color. Only the green or blue color is to be considered positive. I have used larger portions of normal feces with negative results, but the importance of using small quantities of the reagent has been pointed out.

In the series of 100 feces the guaiac, aloin, and benzidin tests were carried out, in addition to the routine feces examination. I thought at one time in the study that the composition of the feces might play an interfering role in the tests, but I found the tests positive or negative, as the case might be, irrespective of reaction, bile pigments, fat, vegetable fibers, and very often meat. Of the

[14] It was found to be more convenient to pour the ether from the large test tube, than from a separating funnel, as in the latter method it is almost impossible to remove more than half of the ether.

[15] Amer. Jour. Med. Sci., July, 1905.

100 cases some have been examined a number of times, and in all I have studied 129 feces. In order to avoid long tables of diet, microscopic and chemical findings, and diagnoses, I shall confine myself simply to a tabulation of the comparative results given by the three tests.

Aloin, guaiac, and benzidin positive	28 times.
Aloin, guaiac, and benzidin negative	82 "
Aloin positive, guaiac and benzidin negative	0 "
Guaiac positive, aloin and benzidin negative	0 "
Benzidin and guaiac positive, aloin negative	5 "
Benzidin positive, aloin and guaiac negative	2 "
Benzidin and aloin positive, guiaac negative	2 "
Benzidin and guaiac positive, aloin?	3 "
Benzidin and aloin positive, guaiac?	1 "
Benzidin and guaiac negative, aloin?	2 "
Benzidin and aloin negative, guaiac?	1 "
Aloin and guaiac negative, benzidin?	1 "
Aloin, benzidin, and guaiac?	2 "

In all, the three tests agreed 110 times out of 129 stools examined, whence I have no hesitancy in proclaiming the benzidin test an important addition to our laboratory equipment. From these studies I should advise first a test of the feces with benzidin; if negative we may be sure of the absence of blood, and we need go no further. If, on the other hand, the test is positive, the aloin and guaiac tests should be made, and if these are negative, occult blood may be regarded as being absent. A substantiation of the benzidin test by either the aloin or the guaiac test is to be regarded as indicating the presence of blood. Hence, a positive benzidin test shows nothing unless corroborated by one or both of the other tests; a negative test, however, is proof positive of the absence of occult bleeding. (In none of the cases was the benzidin test negative and the other tests positive.)

The clinical importance of a positive or a negative blood test is well known, has been dilated upon by various writers, including Steele, who made the first observations in the United States. At present I can add nothing to what has been already said.

I have also tried the benzidin test on gastric contents and the urine. Meanwhile, Schlesinger and Holst have reported their observations on the applicability of the test in detecting occult blood in the urine. For this they advise 10 c.c. urine + 0.5 to 1 c.c. of glacial acetic acid, invert a couple of times, then add one-third volume of ether and shake well. After standing a short time one can make a sharp separation by the addition of 5 to 10 drops of absolute alcohol and gentle shaking. If no separating funnel has been used, the ether may be drawn off with a pipette, and this extract treated with benzidin and H_2O_2 in the usual way, a green to a blue color indicating blood. They claim that the benzidin test is twenty times sharper than Heller's, and five times as sharp as the guaiac or the aloin tests, and they prefer it in testing urine for blood.

CONCLUSIONS. The benzidin test is to be recommended unreservedly for feces, gastric, and urine work. The objection to its extreme sensitiveness is invalid, as a control by the other tests may be made; while that very objection supports my assertion that if the benzidin test is negative the specimen may be considered free from blood. I advise checking a positive reaction with either the guaiac or the aloin test, preferably both.

2. The reasons given for advising the benzidin test as given by Schlesinger and Holst are sufficient, and need no further discussion.

3. Only the Merck benzidin puriss. should be used.

4. The quantities of the reagents must be carefully observed and the test tubes must be clean.

5. All disturbing factors must be first removed. By this I mean inorganic as well as organic. It appears to me as useless to examine a feces repeatedly for occult blood, making no effort to regulate the diet and medication, as it would be to examine the gastric contents chemically after a promiscuous meal, not taking into consideration the time, quantity, and quality of food ingested. Therefore, I advise, if the feces show a positive reaction for blood, that another stool be not examined until the diet and medication have been regulated. Only then can a fair idea of the clinical importance of the test be obtained.

FACTORS INFLUENCING THE EARLY DIAGNOSIS OF GASTRIC CARCINOMA.

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THE advances of the last two decades in the laboratory and clinical diagnosis of gastric carcinoma, combined with the realization of operative possibilities, have been far-reaching, and it is safe to assume will acquire greater importance in the years to come. Following the early workers in the field of gastric analysis and deduction, the work of Billroth stands preëminent, and to the surgeons of our generation much credit is due for urging the necessity of early diagnosis if treatment is to be of avail. One has but to survey the operative results of the Mayos, Senn, Moynihan, Robson, Ochsner, and others to realize how much has been accomplished, and to regard with more hopeful optimism the outlook for the future. On the other hand, there probably will continue to be found much wisdom in the old adage, which refers to making haste slowly, for otherwise surgery will suffer the reaction which always accompanies the less careful diagnosis of cases in the enthusiasm of prospective cure.

The early diagnosis of gastric carcinoma, however, must remain the important factor leading to permanent aid or amelioration, and

it is from this standpoint that I review the pertinent facts. No great amount of value need be placed upon the personal opinions expressed, except in so far as they bring out points for discussion, as to the methods in vogue, from the experience of those interested in the subject.

Carcinoma of the stomach claims a large percentage of those dying from malignancy in general. Judging from the census report of 1900, Dowd[1] states that there were 9000 deaths from carcinoma of the stomach in the United States during that year. This was 65 per cent. more than from appendicitis. McConnell[2] has shown that in the registration area (census 1900) there were 17,296 cancer deaths during that year, of which 4220 were due to cancer of the stomach (24.4 per cent.). Bland[3] has recently stated that typhoid fever has been endemic and epidemic in Philadelphia during the past twenty-five years. During that time scarcely a winter or spring has passed without the city suffering a more or less severe epidemic, and 15,407 persons, including children, died of typhoid fever, while 15,379 died of cancer. In other words, in twenty-five years only twenty-eight more persons, including children, died from typhoid fever than from malignancy in a community where typhoid fever has been unusually prevalent. Cancer of the stomach claimed 37 per cent. of the total number. The comparative immunity of the colored race seems well established; 35.4 times as many in whites as in the colored race (according to McConnell's figures).

One may assume several possibilities in attempting to explain the frequency of carcinoma of the stomach as compared with other parts of the alimentary tract, and the theories, leaving out the possibility of its parasitic etiology as yet unsettled, are speculatively attractive, even if not contributory to definite fact.

Not the least of these has reference to the kind of food and misuse of the organ by practically all the higher animals. The lower animals rarely suffer from gastric ulcer or malignant new growth.

What connection the preponderance of uncooked articles of food may have upon the question would be, indeed, hard to say. The analogy is, perhaps, not a fair one, for, if carried further, the relative immunity of animals to certain other affections common to man justifies in some of us, at least, the belief that such comparisons are not parallel. So this theory of preponderant raw food, with little cooked food in the form of meat, etc., like similar conceptions, is likely to bring one more into a study of fancy than fact, despite the use which has been made of the subject in certain quarters during the past few years.

[1] Facts Concerning Cancer of Stomach, Med. Record, January 20, 1906.
[2] Cancer in United States, Jour. Amer. Med. Assoc., April 28, 1906.
[3] Study of Deaths of Cancer in Philadelphia from 1879–1904, Surg., Gynec., and Obstet., November, 1906.

Our friends the vegetarians have, perhaps, after all established a partial truth, but without justifying their contentions, there can be no question that a simple dietary of cooked and uncooked food such as bread, pressed wheat bread, cereals, milk, eggs, and fats rich enough in caloric value and essential food ingredients, has much to do with the prophylaxis of gastric disease and abuse which a vast majority of individuals give to the stomach. The chow-chow, pickles, bizarre salads, hot breads, hot pies, etc., were assuredly the invention of a Mephisto with perfectly functionating gastric secretions.

This abuse of the gastric function concerns faulty mastication, over-eating, the pernicious habit of washing down the food with quantities of ice-water (a habit distinctively American), malnutrition, with resultant anemia from deficient quantity and quality in the case of the poor, and lowered resistance generally. In women other factors are found aside from the necessity of child-bearing, and the many times evident lack of care following delivery.

Prolapsed viscera, and general lack of tone, perhaps with atony and gastric dilatation, and, in delicate women, menorrhagia with secondary anemia, predispose to functional secretory disturbance, which paves the way in many cases to definite alteration of structure in the way of latent ulcer and glandular repair hyperplasias, which may, unfortunately, not stop at the completion of the repair stage; at a later time, they may undergo so-called malignant transformation. These considerations refer in many cases to generally mild, obscure dy peptic troubles with a moderate grade of ptosis or dilatation, extending over years and covered in the phrase "precancer stage" of Murphy, Graham,[4] and others. Many clinicians are of the opinion that a majority of the symptoms are of more rapid onset in gastric carcinoma; still, the latency is marked in a fairly large percentage of cases.

In the history, it is difficult to satisfy one's self as to the influence of heredity (16 per cent. of cases, Dieulafoy;[5] 7 per cent. of all cases, Musser[6]) as compared with other factors mentioned above, general dyspeptic symptoms, latent and frank ulcer, general nutrition, and habits. The belief is expressed that a history of malignancy in some one relative has slight suggestive value only. The possibility of predisposition to malignant change may be considered present and due regard given to it, when two relatives give a positive history. It is surprising, in considering any malady, how large a percentage of families, if careful data are secured, give a so-called cancerous history.

Loss of weight and the age of the patient have only relative importance in early diagnosis. They should, of course, be taken for

[4] Boston Med. and Surg. Jour., August 31, 1905.
[5] Manuel Pathologie Interne, ii, 190.
[6] Trans. Coll. Phys. Phila., Noevmber 13, 1905.

what they seem worth, together with the general symptom complex. Many patients with chronic functional secretory disturbance are markedly emaciated and profoundly asthenic. If the diagnosis in such cases is not based upon gastric analysis, inflation, etc., and the patient receives guess-work therapy, the guess may as well be wrong as right; and the picture, when the patient presents himself at a later time, is likely to be one of pronounced cachexia.

As regards age, although a vast majority of the patients are over fifty years, carcinoma can hardly be called rare under thirty-five. In a limited experience, I have twice seen the diagnosis confirmed—in one patient at twenty-seven, and the other at twenty-nine years.

Strange to say, gastric carcinoma in early life seems to run a comparatively slow course. Mathieu[7] has reported the case of a man of twenty-five years with symptoms for three years; Catrin, a case lasting two or three years, both quoted by George Dock,[8] who has described a woman, aged twenty-four years, with symptoms for over one year; another woman of twenty-one years, with symptoms for nine months, and tumor for six months before death; and a man of twenty years, with symptoms for one year.

Primary sarcoma and myoma in the 62 or 63 cases on record has usually occurred in young individuals of seventeen to twenty-five years. A recent article by Lecéne and Petit[9] mentions as the most common form a large tumor, which may be pedunculated, projecting into the abdominal cavity. It may produce no symptoms on the part of the stomach, merely suggesting an abdominal tumor, while again it may simulate carcinoma. Yates[10] has also reported 3 cases from Ochsner's clinic. He concludes that sarcoma is less rare than has been supposed.

Pre-existent ulcer, since the classical publications of Cruveilhier and Rokitansky, has been generally recognized as an important point in the history predisposing to carcinoma. Probably more stress has been laid upon this point than is generally warranted.

Dittrich of Prague, in 1848, reported 160 cases in which ulcer and carcinoma were associated 8 times; Lebert reported 100 cases preceded by ulcer in 9; Rosenheim reported ulcer and carcinoma in 6 cases in 100; Sonicksen, 14 in 100; Graham, in 135 cancer cases, found a history of ulcer in 60 per cent.

Carcinoma undoubtedly occurs in those areas of the stomach wall most frequently the site of ulcer: in order of frequency, the pylorus and the posterior wall of the lesser curvature. A smaller proportion originates at the cardia and the anterior and posterior walls of the greater curvature. Ulcer may be present for many years with

[7] La semaine médicale, 1895, 225.
[8] Cancer of the Stomach in Early Life, Amer. Jour. Med. Sci., June, 1897.
[9] Revue de gynecologie, viii, 6.
[10] Sarcoma and Myoma of the Stomach, Annals Surg., October, 1906.

few, if any, classical symptoms, until perforation, hemorrhage, or scar-tissue obstruction is evident. This is especially true if the acidity is low. Riegel's rule that ulcer is almost always associated with excess of acid, had been found misleading. Wagner[11] and many others in approximate confirmation have found that excessive HCl is present in less than half the cases of ulcer; on the contrary, probably 25 per cent. of all cases of ulcer have had excessive HCl secretion at some time.

It is strange, when one considers these facts, that primary carcinoma is not more common upon an ulcer base in the duodenum. Mayo and Franklin,[12] in an experience of 1112 duodenal and gastric operations, have only twice recognized primary carcinoma of the duodenum, and only once developing upon the base of a duodenal ulcer. Still, to quote Dr. Mayo,[13] "ulcer of the duodenum is nearly as common as in the whole of the stomach."

Symptoms. Simple dyspeptic disorders, anorexia, flatulency, and general diffuse abdominal discomfort at the height of digestion, four or five hours after meals, rather than acute local distress soon after eating, seem to be the important early subjective symptoms in most cases. Boas[14] is of the opinion that the symptoms are vague and indefinite in their onset, as a rule.

Vomiting can hardly be called an early symptom. It may be present in a rapidly-growing medullary carcinoma involving the body of the organ or an ulcus carcinomatosa involving the pylorus and leading to early obstruction.

Hemorrhage occurs late, as a rule, except in the cases of malignant change engrafted more or less rapidly upon simple or multiple erosions. The cell character of the neoplasm has something to do with the possibility of hemorrhage, the early tendency to ulceration in the soft encephaloid varieties, and the tardiness, if not complete absence, of hemorrhage in the more densely-growing scirrhus being important factors for consideration.

Pain. In early cases pain is not marked. When present it is usually comparatively late in the disease and is constant, of a dull, boring, heavy character, differing from the periodic or paroxysmal sharp pain of ulcer. Pain as an early symptom of ulcer, with or without associated hyperchlorhydria, is rarely absent, while in carcinoma not involving the pylorus, the patient, at least in a fair percentage of cases, is free from actual pain during the entire course of the disease.

Tumor. When a palpable tumor is present upon inflation, the patient can hardly be considered a subject for early diagnosis. On the other hand, a considerable tumor may be present involving the

[11] Archiv f. Verdauungskrankheiten, xi, No. 1.
[13] Brit. Med. Jour., November 10, 1906.
[12] Jour. Amer. Med. Assoc., September 22, 1906.
[14] Diseases Digest. System. Edit. by Billings (Appleton, 1906).

lesser curvature under the edge of the liver, and give little palpatory evidence even with the advantage of a thin-walled subject. Again, a tumor of the lesser curvature on posterior wall, may be pushed backward upon inflation of the organ and not be palpable.

When palpation is practised after inflation, the possibility should be remembered of the spleen being drawn downward by means of the gastrosplenic ligament, admitting ready palpation and possibly mistake as to the origin of the mass. Retroperitoneal masses may occasionally simulate a growth involving the stomach. Upon one occasion, recalled at the present time, a mass seemingly involving the stomach was shown, upon exploratory incision, to be a displaced kidney.

Likewise, upon another occasion, in an asthenic and cachectic patient, aged sixty-nine years, sick one year with dyspepsia, first examination revealed absence of free HCl, the presence of long bacilli, and lactic acid, together with a readily-palpable mass the size of a small orange in the upper epigastric region, which moved with deep inspiration and appeared to be connected with the stomach. A blood examination, made a few hours later, showed the condition to be one of pernicious anemia with 817,000 red cells. Upon free purgation, the mass disappeared. It was probably due to a distended transverse colon.

Chesnel[15] has mentioned cases of latent carcinoma with no hemorrhage, tumor, or vomiting. I have twice seen at autopsy in elderly individuals, scirrhus carcinoma involving the walls diffusely, but not the pylorus, in patients dying from intercurrent pneumonia, who gave no symptoms except loss of appetite and anemia in the few weeks under observation before death. Stevens[16] has described a case of extensive carcinoma of stomach, liver, and thoracic duct of seventeen months' duration in which there was entire absence of gastric symptoms until the very latest stages. Pitt[17] has also described 17 cases of gastric carcinoma giving symptoms, for the most part, unconnected with the organ (ascites; pleural effusion, 7 cases; matted intestine, 3 cases; obstruction, 2 cases; abdominal suppuration, 2 cases; anemia, 2 cases).

A priori, one would think gastric sufferers would present themselves to the physician earlier than in many other conditions not interfering so much with their feeling of well-being. If this condition of affairs prevailed, it would undoubtedly be of much assistance in the way of early observation of suspected malignant change. Figures, however, in my own cases at least do not show this to be so. I have averaged the length of time symptoms were present in 50 gastric cases before the patient presented himself for treatment and before an analysis was made. The average was about five

[15] Cancer latent de l'estomac. Th. de Paris, 1877.
[16] Brit. Med. Jour., May 29, 1905.
[17] Practitioner, London, April, 1905.

months. Some of these had been treated before, but no analysis of the gastric contents after a test meal had been made.

The suspicion of malignancy in most instances rests upon the ordinary physical examination; but before one can safely exclude malignant change, resort to other useful adjuncts should be secured. In practice, perhaps the majority of physicians do not use the test-meal and the stomach tube. So much has been written relative to the subject, whether one should use one analytical indicator or another, the variety of test meals, the lack of familiarity with sarcines, yeasts, bacilli, lactic acid tests, etc.; in general, the subject has appeared to possess real technical difficulties. For ordinary clinical work much knowledge may be obtained with very little labor, in fact less time than one would consume in making a complete urinary examination.

One may obtain practically all the facts essential to a tentative diagnosis without the use of complicated apparatus. A little practice in reading indicator reactions, in knowing the Kelling, Uffelmann, or Knapp[18] floating ether tests for lactic acid, the microscopic appearance of normal and abnormal gastric elements, and the occult blood tests, would avail much toward the recognition of facts available by no other means.

Too much is expected, as a rule, from one or two examinations. That serious organic disease can be excluded by one or more perfunctory tests is akin to the fallacy of attempting to exclude chronic interstitial nephritis by one or two urinary examinations. The urine may show no albumin for weeks in this most fatal form, while the fact that free HCl is present in the chyme, does not exclude gastric carcinoma or other organic change.

The supposed difficulty on the part of patients in taking the tube is more imaginary than real. A seemingly small chronic ulcer should not contra-indicate its use (symptoms pointing to more or less erosion with evident hemorrhage should probably be contra-indicative). Little trouble need be anticipated in chronic ulcer cases if the procedure is adopted when the tube is half way down the œsophagus of allowing a pint of water to flow down into the stomach in advance of it. Valuable facts may sometimes be secured from these washings.

Complicated analyses, such as it has been my privilege to see occasionally from sanitaria, etc., are rarely necessary. A simplified method of examination suffices: first with an empty stomach in the morning, then with a test meal of one shredded wheat biscuit with 300 c.c. of water removed in fifty minutes (modified Ewald-Boas), and within the next day or two, in order to test the digestive ability under a more tasteful stimulus, the same meal, to which has been added one-quarter pound of chopped beef, broiled, and seasoned

[18] Chyme Analysis, Med. News, New York, November 14, 1903; also Amer. Med., May 7, 1904.

slightly, to be removed in three to three and one-half hours (modified Riegel, or modified Germain-See's). This regime, repeated as often as necessary; inflation of the stomach with an ordinary hand-bulb attached to the end of the tube; and, in thin wall subjects, gastric illumination, will be found quite sufficient.

Despite the controversy concerning the reaction of organic acids to dimethylamido-azobenzol in the test for free HCl, it has been found satisfactory in the vast majority of cases. When organic acid and stagnation are marked, either due to hypochlorhydria or from dilatation secondary to benign obstruction at the outlet (muscular hypertrophy, pyloric spasm, perigastric adhesions with deficient motor power, the scar of an old ulcer) or, malignant constriction, it is better to titrate for free HCl with the dimethyl first; then titrate a separate specimen with a saturated alcoholic solution of tropeolin 00, and subtract the one from the other, the difference being the amount of organic acid present; while the tropeolin titration may be taken as indicative of the amount of free HCl present.

Combined HCl is rarely absent when free HCl is present, and the estimation of the former is rarely necessary in ordinary clinical work. When free HCl is present pepsin or pepsinogen will rarely be found absent. However, the convenient Mette test or egg disk consumes very little time and should be used.

As regards evidence of stagnation in the fasting stomach contents, Ackerman and Gompertz[19] have found that lactic acid and sarcines are supplanted by Oppler-Boas bacilli, and, when abundant, are of much more diagnostic import as indicative of malignant stenosis at the outlet than the finding of sarcines in benign obstruction. With Ziegler's[20] work on the microscopic stagnation of stomach contents as a sign of carcinoma in the lesser curvature, I have had no experience. He contends that the persistence of lactic acid bacilli *after lavage* points to the great probability of carcinoma. In noncancerous cases the stagnation is microscopic or entirely absent, and the lactic acid bacilli are readily removed by one or two stomach washings, while in carcinoma their persistence is the important point, even though the motor function seems to be intact.

There can be no doubt that free HCl is absent, at least when most of the symptoms of malignancy are evident, in a large majority of cases (Wagner,[21] 90 per cent.; Howard,[22] 92 per cent.;). A certain number of cases not infrequently, however, show hyperacidity, especially when the growth is engrafted upon an ulcer, the so-called carcinomatosa.

Recently the very important fact has been brought out by Ben-

[19] Diagnostic Value of the Microscopic Examination of the Fasting Stomach Contents, Med. Record, April 8, 1905.

[20] Ztsch. f. klin. Med., lviii, 6.

[21] Archiv f. Verdauungskrankheiten, xi, 1.

[22] Ulcer of the Stomach and Duodenum, AMER. JOUR. MED. SCI., December, 1904.

jamin Moore[23] and confirmed by Palmer,[24] that there is a marked reduction in HCl secretion in patients with malignant growths, no matter where located in the body, and that this diminished secretion is not dependent upon the location of the growth in the stomach. It has been known for a long time that in the general malnutrition of malignant change involving any part of the body, or from any other cause, the stomach secretions are altered, and that this alteration many times manifests itself in greatly diminished HCl. The work of Moore and Palmer deserves especial emphasis in connection with this subject.

With Sahli's[25] *desmoid reaction* the results are often misleading. Its value, however, is unquestioned in certain cases. The reaction has occasionally been found positive when the secretion of gastric juice was greatly reduced, and again negative with the gastric functions normal.[26]

The detection of *occult blood* in the stools and stomach contents has proved to be of genuine diagnostic worth. The Adler technique (of benzidin in 90 per cent. alcohol, glacial acetic acid, and hydrogen dioxide) has been found absolutely reliable.[27, 28] It shows the presence of blood even in a dilution of 1 to 250,000. Friedenwald and Rosenthal[29] found blood present in practically every case of carcinoma of the stomach examined. To be reliable, no meat should be eaten for two or three days beforehand, and no raw vegetables. Hemorrhoids, the pulling of a tooth, bleeding from the nose or pharynx, occasional intestinal bleeding due to cirrhosis of the liver or tuberculous ulcers, should be carefully excluded.

Occult hemorrhages are never encountered in healthy individuals. Certain forms of cancer, such as the dense slow growing scirrhus, may not be accompanied by occult hemorrhages, but these forms are comparatively rare. With the sensitive Adler technique, Oettinger and Girsuit[30] have found traces of blood frequently in the stools in cases of pure hyperchlorhydria.

Tissue Fragments and Albumin Digestion. As a rule, time spent searching for tissue fragments for microscopic examination in the stomach contents can be better used in other ways. Distinct tumor particles have been occasionally found, but, as a rule, avail one little in the general run of cases. The work of Rosenburg[31] relative to the amount of nitrogenized residue formed from the albumin in the

[23] Proc. Royal Soc., 1905, lxxvi, 138, and Biochem. Jour., 1906, i, 274; Jour. Amer. Med. Assoc., March 2, 1907.

[24] Biochem. Jour., 1906, i, 389.

[25] Corresp.-blatt. f. Schweitzer Aerzte, 1905, xxxv, No. 8-9.

[26] Deut. med. Woch., xxxiii, 1906, No. 22.

[27] La semaine médicale, 1906, xxvi, No. 28.

[28] Deut. med. Woch., 1906, xxxii, No. 36.

[29] Meet. Chirurgical Fac., Maryland, Baltimore, April 24, 1906; also New York Med. Jour., August 11, 1906.

[30] La semaine médicale, 1906, xxxvi, No. 28.

[31] Ztschr. f. klin. Med., 1899, lvi.

cancerous stomach will hardly prove of value in early diagnosis. Normal variations, and especially the variations in the different gastric neuroses, will make the findings uncertain and of questionable utility.

Pyloric Stenosis. Sahli[32] is of the opinion that pyloric stenosis is diagnosticated too frequently, when in reality a somewhat delayed emptying of the stomach may be nothing more than a functional weakness of von Mering's reflex, or slight insufficient motor power. He feels that we are not justified in diagnosticating offhand a pyloric stenosis from the presence in the gastric contents of remains of food taken the previous day.

Gastric Rigidity and Motility. Penzoldt's Iodine Test. The stomach motility in a carcinoma not involving the pylorus may be quite normal. Gastric rigidity has seemed to offer little of value for early diagnosis. The iodine test depends probably as much upon the stomach motility as upon the absorbability of the substance by the mucous membrane. Von Mering[33] has found that potassium iodide is not absorbed at all by the stomach in the dog even after two or three hours, and that the potassium iodide is absorbed almost solely by the intestine.

Enlargement of the Supraclavicular Glands. Enlargement of the glands near the attachment of the sternomastoid muscle on the left side especially has been considered a sign of a certain value in gastric carcinoma. Such enlargement may be difficult to tell in early cases from simple inflammatory resection due to other causes. It has been found present also in cases of ulcer of the stomach.[34]

Trousseau laid great stress upon an *obliterative phlebitis* as one of the early signs of gastric carcinoma. In fact it was the appearance of phlegmasia alba dolens which causes him to confirm the diagnosis of cancer of the stomach in his own case and to which he succumbed nine months later.

Elliott[35] is of the opinion that *a Gram-positive stool*, while in no way pathognomonic of carcinoma of the stomach, is still very suggestive of this condition, while a *Gram-negative stool* speaks decidedly against it. The field of study is an interesting one and should be more fully worked up.

Blood Examination. For early diagnosis the blood has no distinctive features in gastric carcinoma. After the process is firmly established the changes found in secondary anemia of moderate grade are usually present. The hemoglobin is reduced to 40 to 60 per cent., in late cases even to 20 to 25 per cent., while the color index remains below 1.0, differing in this respect from idiopathic pernicious anemia or aplastic anemia. The leukocytes, as a rule,

[32] Diag. Methods, 414.
[33] Klin. Jahrb., 1899, vii.
[34] Soc. méd. des Hôpit., January 25, 1895. (Quoted by Dieulafoy.)
[35] Chicago Med. Recorder, June, 1906.

are moderately increased, averaging from 10,000 to 15,000, and this is a very important point in diagnosis. The leukocytosis is of the polymorphonuclear variety.

Exploratory Laparotomy. In a given case, in which simple dilatation is excluded, if evidence of stagnation is present, if under the various test-meals it is found that seemingly permanent secretory alterations have taken place in the way of deficient HCl or excessive organic acids, with the finding of yeasts and long bacilli, and in which the secretion and stagnation are not improved by appropriate medical and dietetic treatment, it is safe to assume that organic disturbance is present. It is not unusual, however, to see a gain of from 8 to 12 pounds shortly after beginning treatment in cancer cases; this, although confusing, should not mislead one in the constant search for evidence of organic disease. Such findings, with or without vomiting, with or without blood, with or without tumor or emaciation, in an individual over forty years, should make one extremely suspicious. Prolonged attempts, to be sure of one's ground from the laboratory standpoint, will lead many times to dangerous delay. One of the apparent reasons why these patients come to the surgeon so late is because of the procrastination so many times evident. Dr. Mayo has found in 313 operative cases that only 26 per cent. were early enough to permit of radical extirpation. These facts should make us more anxious to give such sufferers the benefit of competent surgery, and the whole matter hinges alone upon early diagnosis. "A suspicion of cancer of the stomach, which cannot be disproved by known methods within a short time, should lead to exploration" (Dr. Mayo). This is especially true if there is a chronic ulcer element present in the history, with return of dyspeptic symptoms not amenable to treatment in a few weeks (seven or eight weeks). The presence of icterus, of enlarged clavicular glands, prominent subcutaneous veins over the abdomen, ascites, or more or less constant pain, lessens much the chance of aid, although Robson, Sheldon, and others have mentioned cases supposed to be clearly inoperable, in which recovery has ensued after the temporary drainage expedient, gastro-enterostomy. Such a course of events make it evident that malignancy was not present in the beginning. These border-line cases are difficult of interpretation at best, but when doubt exists, exploration in competent hands should be urged, with the hope that the circumstances after the abdomen is opened will justify procedures leading to permanent aid or amelioration.

DIFFUSE DILATATION OF THE ŒSOPHAGUS WITHOUT ANATOMICAL STENOSIS, WITH THE REPORT OF A CASE DUE TO CHRONIC CARDIOSPASM.

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In 1900 Neuman[1] was able to collect from the literature 70 cases of diffuse dilatation of the œsophagus without anatomical stenosis. In 1904, Mikulicz[2] estimated that at least 100 cases should be collected. The first case on record seems to be that of Purton,[3] in 1821. Huss,[4] in 1842, reported a case in which he made the diagnosis of dilatation of the œsophagus and stenosis of the cardia. At the postmortem he found a dilatation but no stenosis, and he considered spasm of the cardia the cause of the dilatation. Most of the earlier cases were first recognized on the postmortem table, but during the last twenty years a number of cases have been diagnosticated during life.

The early work of Mikulicz and Meltzer has done much to throw light upon the etiology and pathology of this peculiar condition, but as yet it is somewhat obscure. There are several factors to be considered in the etiology. Fleiner,[5] who looks upon the dilatation as congenital and calls it *antestomach* (vormagen) following Luschka, has adopted Mehnert's[6] enteromere theory to explain this. The primary foregut from which the œsophagus is derived is segmented like a rosary and the musculature may be looked upon as consisting of a number of segments, which Mehnert calls enteromeres, separated from one another by a narrow zone or constriction. Each segment corresponds to a vertebra and each narrow zone to an intervertebral disk. There are twelve segments and thirteen narrow zones or constrictions. One segment is below the diaphragm and the rest are above. Fleiner thinks that from an anomaly in development, one or more of these enteromeres may remain, and the muscular fibers, being weak, will give way. Luschka has described a subdiaphragmatic dilatation of the œsophagus, found postmortem, above the cardia, which he calls *antrum cardiacum*. Cases of congenital dilatation seem to be rare. One case of Fleiner's was found accidentally postmortem and there was no history obtained pointing to œsophageal affection.

Zenker[7] mentions a case of a seven months' child, who died when seven days old, in which was found a spherical ectasia, sharply bounded above and below (next to the cardia) by a very thick, bluish-red wall, in consequence of hemorrhagic infiltration. Sievers[8] reports a case with difficulty of deglutition since earliest childhood, which he considers congenital.

Gottstein[9] thinks that in Case No. 15 in his article there was a

congenital dilatation (vormagen), in which catarrhal conditions had come on with consequent cardiospasm. In Case No. 87 in the same article, Gottstein found a subdiaphragmatic dilatation of the œsophagus (antrum cardiacum), spasm of the cardia, and an ulcer on the cardia which later proved to be carcinomatous. Both of these last-named cases were examined with the œsophagoscope.

Primary atony of the muscular coat of the œsophagus as the cause of dilatation, with subsequent cardiospasm, has been described by Rosenheïm and Netter. Netter[10] first called attention to this, but Rosenheim has particularly brought out the importance of this as an etiological factor, chiefly through his œsophagoscopic observations. Rosenheim,[11, 12, 13] describes cases of simple atony of the œsophageal walls, in which the solid food passes very slowly through the tube, causing discomfort, pressure, and pain, but in which there is no stenosis. This in time, however, may give rise to dilatation and cardiospasm. In these cases there is no hindrance to the passage of fluids, and the œsophageal bougie does not meet any obstacle. On examination through the œsophagoscope, the rosette-like folding of the mucous membrane of the cardia is not seen as in cases of cardiospasm. Rosenheim says: To be sure, disturbances of the innervation are at the bottom of this disease, but they are mostly local, and remain local, although general neurosis may be a predisposing momentum, or come on later. Any disturbance in the function of the nerve-muscle apparatus of the œsophagus, especially the cardia, any weakening of the peristalsis, any injury to the cardia, may be followed by ectasia; and what commenced as a simple functional neurosis may end as an irreparable pathological and anatomical process. Rosenheim has also described cases of primary spasm of the cardia without any discoverable lesion. He says that any pathological process in the œsophagus may be accompanied by spasm

Krauss (cited. by Lossen[14]) says that there may be simultaneous atony of the œsophagus and spasm of the cardia, and bases his opinion upon finding degeneration in certain branches of the vagus in a case of dilatation of the œsophagus with cardiospasm.

Zenker considered inflammation of the mucosa as a possible cause of ectasis, and refers to the case of Stern's,[15] in which the mucosa was found greatly hypertrophied, but not the muscular layer.

Martin[16] thinks that inflammation is the important etiological factor in the cardiospasm, and he supports his opinion with the case he reports in which œsophagitis with much secretion of mucus was present from the onset. However, inflammation, ulcers, etc., may be present without giving rise to spasm. Gottstein has observed cases of œsophagitis without spasm and dilatation. Rosenheim mentions 3 cases of chronic œsophagitis with dysphagia, but without any spasm, diagnosticated by the aid of the œsophagoscope.

There was no hindrance to the passage of the sound into the stomach. He also says that there may be œsophagitis without dysphagia. Rosenheim thinks pharyngeal catarrh should also be taken into consideration in diseases of the œsophagus. Ulcer of the œsophagus may be present without giving rise to œsophageal symptoms. Thus, Tileston[17] reports 3 cases of peptic ulcer of the œsophagus, seen postmortem; in the first case there was no symptom referring to the œsophagus; in the second case there was difficulty of swallowing solid food the last few weeks before death; the third case had stomach trouble one year before and gastric pain and vomiting the last two weeks of life.

Mikulicz, and later Meltzer, described cases of dilatation of the œsophagus in which spasm of the cardia was the primary cause. Mikulicz, as early as 1882, according to Gottstein, had observed 6 or 7 such cases and came to this conclusion mainly through the use of the œsophagoscope. Mikulicz gave the condition the name of cardiospasm. As to the cause of the cardiospasm he does not say whether he thinks it due to primary neurosis, œsophagitis, or congenital defect. Meltzer,[18] in 1888, reported a case of this kind. Einhorn,[19] in 1888, reported a case in which he thought a lack of reflex relaxation or opening of the cardia was the cause. Leichtenstern,[20] in 1891, came to the conclusion (independently of Mikulicz) that the spasm of the cardia was the cause of the dilatation with hypertrophy of the œsophagus in a case upon which he made a postmortem two hours after death. Both nervi vagi and branches were examined microscopically and found normal. Kitt (cited by Gregersen[21]) states that dilatation of the œsophagus has been found in horses and sheep and that sarcosporidia were found in the muscle cells. In the majority of the older cases (17 collected by Zenker) that came to postmortem, the dilatation was accompanied by hypertrophy; subsequent cases of similar kind that have come to postmortem are those of Strümpell,[22] Leichtenstern, Rolleston,[23] Johnson,[24] Gregersen, Zinsser,[25] Sippy,[26] Kinnicutt,[27] and Strauss.[28]

The specimens examined postmortem usually reveal a dilatation of the lower two-thirds of the organ, the dilatation having the bottle shape, or is spindle-shaped. The mucous membrane is frequently found inflamed and at times ulcerations are present. The muscular coat, particularly the circular fibers, are found hypertrophied. The small cell infiltration may extend down to the muscular coat. The cardia is mostly found normal, sometimes narrower than usual. In some cases the œsophageal wall is found thinned throughout, or a part of the wall may be thinned and bulging.

According to Neumann, both sexes are about equally affected. Of 41 cases, 22 were in men and 19 in women. Of Rosenheim's 9 cases, all were in men. Most of the cases reported have been between the ages of twenty and forty, but a patient of Fleiner's was seven years old, and a patient of Rolleston's was eight years old.

Gottstein reports a case of acute cardiospasm without dilatation in a child four years old, examined with the œsophagoscope.

The etiology of dilatation of the œsophagus without anatomical stenosis is far from clear, but it seems to me, from a study of a number of cases reported, that the clinical picture varies, and that cases in which atony is primary to the dilatation and spasm, if possible, should be differentiated from the cases in which cardiospasm is primary, as the treatment and the prognosis differ. Gottstein has arranged the cases as follows: (*A*) Cases in which excessive extraphysiological spastic contractions of the musculature take place (hyperkinetic disturbances of motility. (B) Cases in which the contractibility of the musculature is weakened or is entirely lost (hypokinetic disturbances of motility). The hyperkinetic and hypokinetic disturbances are divided according to the etiology into (1) The idiopathic or those in which the organic lesion cannot be demonstrated, and (2) the secondary or symptomatic, that is, those developed in connection with disease causing anatomical alterations, as cancer.

(A) Hyperkinetic disturbances of motility.

Idiopathic.

1. Œsophagospasm, when the spasm involves the œsophagus proper.

2. Cardiospasm, when the cardia is involved.

Cardiospasm—acute, chronic.

A definition of cardiospasm is given by Leichtenstern as a pathological exaggeration of a physiological phenomenon, in which, through an abnormal innervation of the cardia, a habitual, not permanent, spastic closure of the cardia takes place, which is an increase over the normal, lasts for a longer time, and especially takes place after the act of deglutition. Evidently, disturbances of the nervous apparatus of the cardia are at fault, but the question whether the condition is due to failure on the part of the inhibitory nerve fibers controlling the normal tonus of the cardia, or to irritation that has caused an increased tonus in the contracting fibers, may be difficult to determine.

Von Openchowsky[29] found that the vagus nerve contained contracting, as well as dilating fibers, and he demonstrated the brain centres for contraction and dilatation of the cardia. He also found ganglion cells in the serosa of the cardia which have to do with the function of dilatation. If the cardia is cut out of a living rabbit there will be seen rhythmic contractions. The cardia at rest is in a light tonic contraction, and, according to Sinnhuber,[30] the cardia-musculature is strengthened by the surrounding muscles of the diaphragm and the slanting insertion of the œsophagus into the stomach. Sauerbruch,[31] experimenting on dogs, found that the cardia contracted rhythmically synchronous with inspiration, and that the contractions were caused mainly by the musculature of the dia-

phragm. Mikulicz says that there is a valve-like shut-off on the stomach side of the cardia, and cites Gubarow and Kelling. H. Kronecker[32] and S. Meltzer,[33] in their experiments on the mechanism of deglutition, found that fluids were squirted into the œsophagus to the cardia by the action of the mylohyoid muscle, remaining there until the peristaltic wave followed, when they would go through the cardia. Solid food, after being forced into the œsophagus, would be moved forward by the peristaltic wave of the œsophageal walls. The mass would pass the cardia four to six seconds after the act of deglutition. Cannon and Moser[34] found that in man and horse liquids are propelled deep into the œsophagus at a rate of several feet a second by the rapid contraction of the mylohyoid muscles. Solids and semisolids are slowly carried through the entire œsophagus by peristalsis alone. Schreiber,[35] in a recent monograph, differs from Kronecker and Meltzer in regard to the muscles involved in the act of swallowing. Schreiber says that the mylohyoid muscle, when the mouth and nasopharynx is shut off, throws the food into the pharynx, where the constrictor media muscles and others press the bolus down into the œsophagus. He also says that the constrictor inferior antagonizes the swallowing muscles, as it holds the upper end of the œsophagus in a tonic closure; and that, when the food has passed into the œsophagus, the constrictor inferior closes after it. Schreiber found that fluids are not squirted down to the cardia, but are moved by peristalsis, like solid food. Mikulicz differs from Kronecker and Meltzer in regard to the passage of fluids. From experiments he found that fluids, after being pressed into the œsophagus, by their own weight, will open the cardia automatically without the aid of peristalsis. Mikulicz thinks that the ganglion cells in the cardia serosa have to do with the automatic opening on light pressure. Irritating fluids, as very hot or very cold, and irritating chemical fluids, make an exception to this, as they may cause an increased contraction of the cardia.

The œsophagus, on an average, is 25 cm. long, and, according to Mehnert and Mikulicz, is a straight tube. There are usually one or more physiological constrictions of the organ present, and the ones at the commencement and at the tracheal bifurcation and at the end are those most frequently found. Mehnert found in 50 per cent. of bodies that the œsophagus increases in width from above down, and he gives v. Hacker's measurements as 13 mm. diameter at the commencement, gradually increasing to 22 mm. in diameter above the cardia. Mikulicz found the diameter in the upper two-thirds to be 16 mm., in the lower one-third, somewhat narrower. The capacity of the organ varies from 40 c.c. to 80 c.c., but even 150 c.c. may be within physiological limit, according to Rumpel. The tube is closed in the neck part, but is open, and contains air in its passage through the chest (Mikulicz, Rosenheim,[36] and Chiari). According to Morosow,[37] the average distance from

the incisor teeth to the commencement of the œsophagus in adults is 14.8 cm. The average distance from the incisor teeth to the cardia is, according to Rosenheim, 39.9 cm. in men and 37.3 cm in women. The position of the cardia changes with age; in the newborn it is found at a level with the eighth dorsal, and in old people may be as low as the twelfth dorsal vertebra, the average being between the ninth and eleventh. The cardia and œsophagus sink somewhat when the stomach is loaded. Mikulicz[38] and Schlippe[39] have made a number of observations on the intraœsophageal pressure. Mikulicz found that the pressure during rest is a trifle below the atmospheric pressure. By quiet inspiration the pressure is lowered to —9 cm. water pressure, and by forced inspiration to —20 cm. or below. On quiet expiration the pressure goes up to +10 cm. water pressure, and by forced expiration to +20. By coughing, the pressure may be 60, 80, or even 160 mm. mercury. On deglutition the pressure varies between 0.80 and 22 cm. water. The normal cardia opens easily without the aid of deglutition for fluids and gases going from the œsophagus into the stomach, but with difficulty in the reverse direction. The pressure necessary to open the cardia from the œsophageal side ordinarily amounts to a fraction of the pressure of a column of water filling the chest part of the œsophagus. When irritating fluids, as carbonized fluids or very hot or very cold fluids, are taken the pressure is higher.

If, now, the resistance of the cardia is increased, a part of the fluid swallowed will remain in the œsophagus. Suppose that, to effect the automatic opening of the cardia under normal conditions, a pressure of 12 cm. water pressure is necessary. In that case the balance of the fluid above the 12 cm. would flow into the stomach by its weight, leaving behind a 12 cm. column of fluid. This would be carried into the stomach by the pressure caused by the following act of deglutition, which corresponds to about 12 cm. water pressure. It the resistance of the cardia corresponds to 24 cm. water pressure, there will be left a column of 12 cm. at the end of the act of deglutition. If the resistance on the part of the cardia is still higher, only so much fluid will pass the cardia as is pressed down by the pharyngeal musculature. The œsophagus itself can only overcome the resistance of the cardia when it by energetic contraction can raise the pressure correspondingly. As long as the œsophagus has its normal dimensions the effect of the pressure is comparatively small, but when the organ becomes more dilated, so that the area upon which the pressure can be exerted is considerable, the dilatation increases more rapidly. The secondary changes in the œsophageal wall brought on by the stagnating ingesta may add to the increasing rapidity with which the dilatation takes place.

Mikulicz thought that the information gained by measuring the intra-œsophageal pressure in cases of dilatation would be of great value in diagnosis, as well as clear up the etiology. The pressure

during deglutition would be an indicator of the condition of the contracting power of the muscular wall of the œsophagus. The apparatus used is very simple and consists of a rubber tube connected with a manometer. He reports 3 cases in which the pressure was estimated in this way. The following is the history of one of my cases:

Mr. H. B. E., aged twenty-seven years, unmarried, clerk, was seen January 17, 1907. Father well, mother nervous, brothers and sisters well. The patient had measles when a child and bronchial cough during the winter months from the age of ten to fifteen; otherwise his health was excellent. No specific history. He has always been in the habit of eating fast. He never had any throat trouble until the age of seventeen, when he had an attack of sore throat and swollen tonsils. During this attack, while at the dinner table, he was taken with a choking spell, turned blue in the face, and was not relieved until the food had come back. From now on he had difficulty in getting the food into the stomach, and in the course of two weeks the present condition was fully developed. Present complaints: when the patient has eaten about one-fourth of his meal he has a sensation of choking back of the larynx, and he is obliged to take a large quantity of water, 300 to 400 c.c., to force the food down. If he does not succeed in getting it down, all the food and the water come back. He repeats this three, four, or five times during the meal. Sometimes he feels that the food commences to pass into the stomach while he is drinking the water, at other times not. He always gulps up some of the water used to force the food down. At some meals nearly all the food and water come back, and he has to leave the table unsatisfied. If he drinks between meals, the water is always regurgitated. Very hot or very cold drinks increase the difficulty. He takes only two meals a day because he cannot get home to his midday meal, and he does not want to go through the performance in a public place. At times he will wake up in the night with what he calls a "contracting pain" to the right of the base of the ensiform process. If he then takes a drink of water and gulps it up again he feels relieved. Of late he has taken a small quantity of whisky and let it remain, with relief. He never found that any food or drink had run out through his mouth or nose during sleep. At times the "contracting pain" will come on on swallowing anything, solid or fluid.

During the first part of January of this year the patient was worse than usual, and he could only get very little food down for four or five days. Ever since this dysphagia commenced it has never left him, but at times he has had but little difficulty. He is particularly bad when he has a cold or when he has to work hard, or if he worries. In the first part of December, 1906, he was sick with ptomaïne poisoning and tried to vomit, but he did not succeed. He had his tonsils removed years ago.

Examination: Slight catarrhal pharyngitis. Bloodvessels, heart, and lungs negative. On introducing a soft stomach tube it meets resistance at 15 cm. from the incisor teeth, and the patient has a choking spell; it is difficult for him to get his breath. After several attempts the tube was passed. There was evidently a spasm of the upper end of the œsophagus, which was noticed on every subsequent examination. The tube now passes readily down to 42 cm., when another obstacle is met with, and it is necessary to use a wire stylet in the tube. After gentle pressure is exerted for some time, the cardia suddenly gives way and the tube passes into the stomach. The stomach was inflated with air and found of normal outline. I found that the patient could drink 410 c.c. water and regurgitate it all after a few minutes. At one time he regurgitated 425 c.c.; the excess was mucus. This amount could be siphoned off from the œsophagus. After a test meal of toast and water, drawn off one hour later, I first obtained masses of bread enveloped in mucus from the œsophagus; when the tube was passed into the stomach by the aid of the stylet, the contents differed in appearance. The œsophageal contents was alkaline in reaction. The contents of the stomach showed normal acidity. On the introduction of the œsophageal bougie there was a violent spasm of the upper œsophagus and the bougie was passed with difficulty. Through the cardia it passed without hindrance. It was my intention to examine through the œsophagoscope, but I had to desist on account of the great irritability of the upper end of the œsophagus. For the same reason I could not use the double tube test of Rumpel to differentiate between dilatation and a deep-seated diverticulum. I used instead a modified Rumpel test suggested by Starck (cited by Kramer-Peterson[40]). The ordinary stomach tube was passed into the stomach and 750 c.c. of water poured in. The patient was then given 250 c.c. of milk to drink (with the tube in situ). The water was now allowed to flow off from the stomach and it returned clear. The tube was then pulled into the œsophagus and the milk was siphoned off. All the milk was recovered except 10 c.c. I now introduced with the stylet a stomach-tube to the end of which was attached a thin rubber bag covered with a silk bag, which, when distended, had a pear shape, and had a diameter of 3.75 cm. This was distended with water and could be moved up and down in the œsophagus for several centimeters. A larger size, 5 cm., was then used. I found that this could be moved only slightly, so I concluded that the dilatation was about 5 cm. in diameter. The swallowing sound was not heard at the ensiform process. After giving the patient 20 per cent. bismuth in thick oatmeal gruel, *x*-ray pictures were taken, but they were not satisfactory.

Diagnosis: Diffuse dilatation of the œsophagus, due to cardiospasm (and œsophagospasm). The diagnosis was based on the sudden onset with regurgitation of food and fluids; the fact that at times

he had little difficulty in passing the food into the stomach, while at other times he could not get anything down at all; the hindrance to the passage of fluids from the onset; the peculiar sensation in passing the stomach tube with the stylet or the bougie; the sudden giving way of the cardia on gentle pressure; the ease with which the tube could be passed at times, and the difficulty encountered at others; the result of sounding with the pear-shaped rubber-silk sound; the capacity of the organ 425 c.c. The history would exclude cancer or other growth; the absence of a history of swallowing caustics, and the ease with which the large-sized bougie could pass the cardia, excluded benign stricture. The result with the modified Rumpel test excluded diverticulum, and so did the fact that the tube or bougie never entered a pocket; the resistance met was always at 42 cm. from the teeth, and it could always be overcome by gentle pressure without changing the position of the tube. There was never any food found in the œsophagus from the previous day's meal; the contents of the œsophagus was alkaline or neutral.

To exclude primary atony, the regurgitation of fluids from the start, the sudden onset, the promptness with which the patient could eject the contents of his œsophagus, aided. This latter fact, and the comparatively little pain in this case would rather lead one to think of dilatation with hypertrophy and with very little inflammation of the mucosa. That the inflammatory condition of the patient's throat and tonsils had been an exciting cause seemed quite reasonable. There must, however, have been an abnormally excitable condition of the nervous mechanism of the œsophagus and cardia present.

Prognosis has been considered grave in these cases, but the results gained by overstretching the cardia in cases of pure cardiospasm are more promising, although cases have, perhaps, not been observed long enough after treatment to judge if the cure will be permanent.

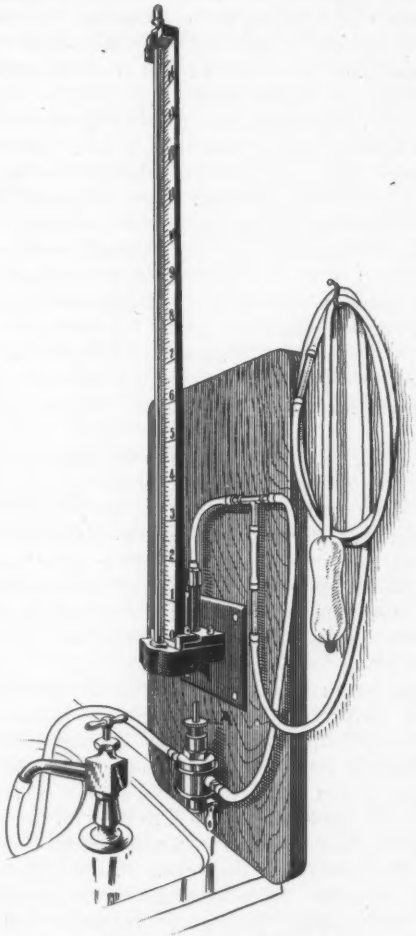
February 23. Dilated the cardia with rubber-silk bag dilators, using first one with a diameter of 1.5 cm., then the next size, 2.2 cm., under six pounds pressure. Patient felt the "contracting pain" when the larger size was used.

February 26. Dilated the cardia with the 2.20 cm. size, followed by the largest size, 3.00 cm., under eight pounds pressure. Patient complained of the same "contracting pain."

During the first week after the last treatment the patient regurgitated a mouthful of fluid three or four times, during the second week only once, and since then has been perfectly well and has gained twenty pounds up to the time of writing this paper.

The pronounced œsophagospasm in this case makes it rather unique. At times when I introduced the stomach tube the spasm of the œsophagus would be so severe that the patient's face became deeply congested and he could not get his breath for quite awhile,

when it would come in a long-drawn whoop. When the tube had passed into the chest part of the organ it would be pushed down to the cardia with perfect ease, and the patient could drink while the tube was in place without any trouble. I frequently had to use the



Apparatus for dilating the cardia.

wire stylet to stiffen the tube to get through the upper part of the œsophagus, and at times I made several attempts before I succeeded in getting through.

In order to be able to dilate the cardia with a gradually increasing

pressure, that could easily be controlled, I constructed an apparatus as follows: Between the water faucet and the quicksilver manometer, connected by rubber tubing, I inserted a pressure regulator. Between the regulator and the manometer a T-tube was inserted, the one limb of which was connected by a long rubber tube to a stomach tube having at the distal end the rubber-silk bag, as suggested by Russell[41] in 1898 (a thin rubber bag is attached to the end of a stomach tube and covered with a sausage-shaped silk bag 10 to 12 cm. long). In operating the apparatus the regulator should be set on the lowest pressure, the pressure gradually being raised by turning the screw *A* slowly from right to left. (See figure.)

To dilate the cardia forcibly in the dark is not entirely without danger, and Mikulicz and Naunyn[42] have expressed themselves to that effect, but there have been no reports of deaths from the procedure as yet. If the dilatation is gradually performed, and the pressure is under perfect control, the danger is small. A sudden high pressure would undoubtedly be dangerous, but I think this danger has been overcome by using the pressure regulator as indicated in my apparatus. The use of bougies for dilating the cardia does not give good results and are not without danger, as death from perforation with subsequent mediastinitis has been reported.

Gumprecht, cited by Strauss, says that the maximum to which the normal cardia and œsophagus can be dilated is, respectively, 3 cm. and 3.5 cm. When the expansibility of the dilator is limited and of known dimensions, the amount of pressure used is of less importance, provided the increase of pressure is gradual. When the rubber-bag dilator is not guarded the maximum amount of pressure that can be used with safety must be known. Schreiber found that the normal cardia from the stomach side could resist the pressure of 350 grams for a few seconds.

The use of the *x*-rays in making diagnosis in a number of cases has been of great help, but Rosenheim says that *x*-rays cannot always be depended upon in making a diagnosis in these cases, and that it certainly cannot take the place of the other diagnostic means in making the differential diagnosis. Krauss, cited by Richartz,[43] is of the same opinion. G. Rosenfeld, cited by Strauss,[44] used a thin rubber bag attached to a stomach-tube, which was introduced into the œsophagus and filled with the bismuth mixture in taking *x*-ray pictures. In order to determine the size of the dilatation of the œsophagus, Strauss introduced a thin rubber bag attached to a stomach tube and distended it with air. He then measured in a eudiometer the quantity of air used. Mikulicz's instrument to determine the width of the œsophagus is constructed on a plan similar to that of the Otis urethrometer. The pear-shaped rubber-silk bag sound which I used to determine the width of the œsophagus differs from Russell's dilator only in the shape of the

silk bag and in that the stylet has to be in to make it stiff. The use of this instrument for sounding was suggested by Plummer,[45] who used oval silk bags.

Rosenheim and Wilms[46] have used a rubber bag attached to a stomach tube, but without silk cover to dilate the cardia (a modified Schreiber's sound), using water pressure. Strauss used air pressure to distend the rubber bag for dilatation, and he had his manometer so arranged that not more pressure than 250 cm. mercury could be brought upon the cardia. Jacobs,[47] of Antwerp, in 1898, constructed an apparatus on the plan of a urethral dilator with which he stretched the cardia to a diameter of 3.5 cm. Mikulicz has reported 4 cases in which he did a gastrotomy and stretched the cardia with a specially constructed forceps under the guidance of the fingers. Erdmann[48] reports a case treated in a similar way. Sounding without end was recommended by Lotheisen, cited by Langemak,[49] and was used by Martin in his case. In one of the cases reported by Gottstein a hard rubber tube, with a valve in the lower end to prevent regurgitation from the stomach, was left in the cardia. Jaccoud[50] mentions that Broca dilated a spasmodic stricture of the œsophagus successfully with a forceps. Cahn[51] has made use of a soft rubber tube, into which he poured mercury to dilate the cardia.

The use of the œsophagoscope will become necessary in some of the cases of cardiospasm in order to clear up the etiology, since the spasm may be secondary to ulcer or cancer of the cardia or œsophagus, and it would be rather unsafe to dilate a cardia in the presence of an ulcer.

I will include the history of another case, that is rather interesting, because there seems to be an element in the early history of the patient that points to the possibility of it being of congenital origin. As I only had the opportunity to see the patient twice, I could only make a preliminary diagnosis.

Mrs. B. S., aged 21 years, was seen January 4, 1906. Menses commenced at thirteen, always regular. One child, two years and six months old. Family history negative. She had measles, chickenpox, and whooping-cough when a child. Was never perfectly well. She had much trouble with her stomach in babyhood, and she was weak and puny. At the age of ten years she was taken out of school on account of epigastric pain and belching of gas. She never vomited or regurgitated her food at that time. From this time and until two months before her baby was born she did not have any particular trouble with her stomach. She never felt strong and well, however, and was treated for chlorosis. The present trouble began two months before the baby was born (in June, 1903). She had no morning sickness or vomiting in the first part of her pregnancy, and her appetite was good; but she commenced to experience distress, fulness, and some pain after

eating, and later she began to regurgitate her food while eating. This condition has remained ever since. She says that she a ways regurgitates it and never vomits. The patient feels that the food does not enter the stomach. After she has regurgitated it she eats again, and the regurgitation may be repeated or the food may pass into the stomach, and better if she presses with her fingers in the epigastrium. There is a sensation of choking, oppression, or fulness in the chest on eating; she refers this sensation to a level above the diaphragm. Occasionally she is wakened in the night by slime and particles of food coming through the nose, causing a burning sensation. If she drinks water in the ordinary way it comes back immediately. She has to sip it. There is no particular food that she can take better than others. Whatever food gets in her stomach agrees with her. She never vomited blood.

January 5. I introduced the stomach tube about 12 o'clock today and drew off a considerable quantity of mucus mixed with food. In this material I found spinach that she had had for dinner the previous day. Examination of contents showed absence of hydrochloric acid and presence of lactic acid. On introducing the stomach tube it did not give the impression of entering the stomach, but it bent upon itself. Only a small quantity of air or water could be introduced before the patient gave evidence of pain.

My preliminary diagnosis was diffuse dilatation of the œsophagus or a deep-seated diverticulum. I did not have the opportunity to see the patient again. The history of this case points to dilatation of the œsophagus with cardiospasm, but the finding of spinach in the œsophagus from the previous day's meal brought the question of a low-seated diverticulum strongly into prominence. If there was not a diverticulum present, there must be either a pouch-like bulging of one part of the wall of the œsophagus or a circular gutter, as mentioned by Tyson,[52] caused by the dilated extreme lower end of the œsophagus, spreading out over the dome of the diaphragm, and in which the spinach in this case could lodge while other food had passed through. From the study of the history and limited examination of the patient, I was in favor of the latter explanation; but, diverticulum would have had to be excluded by further examination. We have here a young woman who had much trouble with her stomach when a baby and early childhood, and who had to be taken out of school at the age of ten on account of epigastric pain and belching; and then at the age of eighteen, during the latter part of her pregnancy, began to get fulness, distress, and pain after ating; and later, suddenly had an attack of cardiospasm with eourgitation of food, which condition has become chronic. It is only two years and a half since the regurgitation commenced, and yet there seems to be a considerable dilatation, which shows that there must have been considerable weakness of the wall, or that the condition is like that of Case No. 15 of Gottstein's, referred to above,

in which a congenital dilatation, a catarrhal condition, had come on with subsequent cardiospasm.

I do not know of any method by which a congenital dilatation can be differentiated, except by early œsophagoscopic examination. The mere fact that the patient had much stomach trouble in babyhood and at the age of ten, does not entitle one to draw the conclusion that the case is congenital, but the history in connection with the rather pronounced dilatation which seems to be present would tend to draw the attention to congenital dilatation.

There are very few cases of dilatation of the œsophagus without stenosis reported in the American literature; besides, those above referred to I have only found the case of Liebmann,[53] in 1892, Einhorn's[54] cases in 1900, Tyson's in 1904, and Pummer's in 1906.

BIBLIOGRAPHY.

1. Neumann. Ueber die einfach gleichmässige Erweiterung der Speiserohre., Centralbl. f. d. Grenzgeb. d. Med. und Chir., 1900, iii.
2. Mikulicz. Zur Pathologie und Therapie der Cardiospasmus, Deut. med. Woch., 1904, Nos. 1 and 2.
3. Purton. Lond. Med. and Phys. Jour., 1821, xlvi.
4. Huss. Hygiea, Stockholm, 1842, cit. by Johnson, Band iv.
5. Fleiner. Neue Beiträge zur Pathologie der Speiserohre, Münch. med. Woch., 1900, Nos. 16 and 17.
6. Mehnert. Ueber die klin. Bedeut. d. Œsophagus und Aortenvariationen, Arch. f. klin. Chir., 1899, Band lviii.
7. Zenker and v. Ziemssen. Cyclop. of the Pract. of Medicine, 1878.
8. Sievers. Saakaldt Idiopatisk Œsophagus Dilatation uden paaviselig Stenosis. Hospitaltidende, 1902, No. 39, Kjobenhavn.
9. Gottstein. Technik und Klinik der Œsophagoscopie.
10. Netter. Ueber Erweiterung der Speiserohre im unterem abschnitt. Arch. f. Verdauungskrankheiten, 1898, Band iv.
11. Rusenheim. Ueber Spasmus und Atonie der Speiserohre. Deut. med. Woch., 1899, Nos. 45, 46, 47.
12. Rosenheim. Beiträge zur Œsophagoscopie. Deut. med. Woch., 1899, Nos. 4 and 5.
13. Rosenheim. Ueber Erweiterung des Œsophagus ohne anatomische Stenosis. Berliner klin. Woch., 1902, Nos. 11, 12, 13.
14. Lossen. Ueber Idiopathische Œsophaguserweiterung. Deut. med. Woch., Band xxix, Berl. Beil., 94.
15. Stern. Arch. f. Heilkunde, 1876, Band xvii. Cit. by Zenker and Neumann.
16. Martin. Zur Chir. Behandl. des Cardiospasmus and d. Spindelförmige Speiserohrenerweit. Mitt. a. d. Grenzgeb. d. Med. und Chir., 1901, Band viii.
17. Tileston. Peptic Ulcer of the Œsophagus, Amer. Jour. Med. Sci., August, 1906.
18. Meltzer. Ein Fall von Dysphagie. Berl. klin. Woch., 1888, No. 8.
19. Max Einhorn. A Case of Dysphagia with Dilatation of the Œsophagus. Med-Record, December 29, 1888.
20. Leichtenstern. Beiträge zur Pathologie des Œsophagus. Deut. med. Woch., 1891, Nos. 14 and 15.
21. Gregersen. Ein Fall von s. g. Idiopath. Œsophagusdilatation. Nord. Med. Arch., 1903, Afd. ii, No. 1.
22. Strümpell. Deut. Arch. f. klin. Med., 1881, Cit. by Leichtenstern.
23. Rolleston. Brit. Med. Jour., December 7, 1895.
24. Johnson. Likformig Dilatation of Œsophagus, Hygiea, Stockholm, 1895, Band lvii.
25. Zinsser. Ein Fall von Spindelf. Erweiterung d. Speiserohre. Münch. med. Woch. 1902, No. 52.
26. Sippy. Idiopathic Dilatation of the Œsophagus. Trans. Assoc. Amer. Phys. 1904, xix.

27. Kinnicutt. Idiopathic Dilatation of the Œsophagus. Trans. Assoc. Amer. Phys., 1904, xix.

28. Strauss. Berl. klin. Woch., 1902, No. 14.

29. v. Openchowski. Ueber die Innervation der Cardia durch die Nervi Pneumogastrici. Centralbl. f. die Med. Wissenschaft., Berlin; 1883, Band xxvi, also, Arch. f. Anatomie u. Physiol., 1889.

30. Sinnhuber. Beiträge zur Lehre von muskularen Cardiaverschluss. Zeitschr. f. klin. Med., Band l, Heft 1 and 2.

31. Sauerbruch. Zur Frage des Cardiaverschluss des Speiserhore. Deut. med. Woch., 1906, No. 31.

32. Kronecker und Meltzer. Der Schluckmechanismus, seine Erregung und seine Hemmung. Arch. f. Physiol., Supplementblatt zum Jahrgang, 1883. Cit. by Mikulicz.

33. Meltzer. A Further Experimental Contribution to the Knowledge of the Mechanism of Deglutition. Jour. Exper. Med., 1897, ii, No. 5.

34. Cannon and Moser. Movement of Food in the Œsophagus. Amer. Jour. Physiol., 1898, No. 4.

35. Schreiber. Ueber den Schluckmechanismus. Berlin, 1904.

36. Rosenheim. Ueber die Besichtigung der Cardia nebst Bemerk. über Gastroskopie. Deut. med. Woch., 1895, No. 45.

37. Morosow. Dissertation, 1887. Cit. by Mehnert.

38. Mikulicz. Beiträge zur Physiol. der Speiserohre und der Cardia. Mitt. aus. d. Grenz. d. Med. u. Chir., Band xii, Heft 5.

39. Schlippe. Physikalische Untersuchunpen bei der Anwendung des Magenschlauches, Deut. Arch. f. klin. Med., 1903, Band lxxvi, Heft 4 und 5.

40. Kramer-Peterson. Om den Diffuse Œsophagusdilatation. Ugeskrift for Läger, 1905, No. 13.

41. Russell. Brit. Med. Jour., June 4, 1898.

42. Naunyn. Deut. med. Woch., 1904, No. 43, v., s. 1597.

43. Richartz. Ueber die Differential Diagnosis zwischen Spindelform. Erweiterung u. d. divertikel. Deut. med. Woch., 1904, No. 20.

44. Strauss. Zur Diagnosis u. Therapie d. Cardiospastische Speiserohrenerweiterun. Berl. klin. Woch., 1904, No. 49.

45. Plummer. Jour. Minn. State Med. Assoc., October 1, 1906.

46. Wilms. Berl. klin. Woch., 1904, No. 42.

47. Jacobs. Annales de la Soc. de méd. d'Anvers. November and December, 1898. Cited by Strauss.

48. Erdmann. Annals of Surgery, 1906, xliii.

49. Langemak. Spastische Erkrankungen des Magen-darmtractus. Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1902, v.

50. Jaccoud. Tráite de pathologie interne. Paris, 1877.

51. Cahn. Ueber die Diagnostiche Verwertung der Röntgenstrahlen u. d. Gebrauch d. quicksilber Sonde bei Speiseröhrenerkrank. Münch. med. Woch., 1906, No. 2.

52. Tyson, Martin, and Evans. Diffuse Dilatation of the Œsophagus due to Cardiospasm. Trans. Assoc. Amer. Phys., 1904, xix.

53. Liebmann. A Case of Dysphagia with Dilatation of the Œsophagus. Boston Journal, 1893.

54. M. Einhorn, Amer. Jour. Med. Sci., 1900, cix and cxx.

PANCREATIC LITHIASIS, WITH CHRONIC INTERSTITIAL PANCREATITIS, FOLLOWED BY DIABETES MELLITUS.

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The recognition of pancreatic disease from the clinical symptoms is, on the whole, of rather rare occurrence, typical examples of this condition for the most part being found only at autopsy. We consider ourselves especially fortunate, therefore, in having been able to follow a case more or less throughout its entire course. Pancreatic calculi have been noted for many years—according to Oser—since the middle of the seventeenth century; nevertheless, the clinical recognition of the condition still remains in more or less obscurity, unless pancreatic stones are found in the stools, despite the recent efforts that have been made by Hewlett, Edsall, Schmidt, Cammage, and others, to discover definite changes in the secretions and excretions of the body. The pathological alterations of the pancreas, due to duct obstruction, have been noted by various observers, and the relationship of pancreatic disease to fat necrosis, on the one hand, and to diabetes mellitus, on the other, offers a fertile field for investigation if necessary.

The case is as follows:

H. S., married, a coachman, was admitted to the University Hospital, June 2, 1905, complaining of "pain in the upper abdomen, nausea, and vomiting." The family history was without interest. The patient had had no serious illness that he could remember. He claimed to have had a long series of malarial attacks six years previously, from which he made a perfect recovery. He had also had measles and grippe, but not typhoid fever. An accident, which befel him six years previously, is of interest, insomuch as it may possibly have some bearing on the condition; he was thrown violently from a horse, and received a severe blow in the abdomen; this was followed immediately, and for the subsequent three days, by nausea and vomiting, the vomitus containing some blood on several occasions; there was also a history of melena. These symptoms subsided in a week or ten days, and did not return.

The dyspepsia and abdominal pain, for which the patient applied for relief, had come on insidiously, about eighteen months previously, and they were described as paroxysmal rather than as continuous, each attack being rather more severe than the one before. The present one dates back about two weeks, and was chiefly char-

acterized by abdominal pain in the upper quadrants, associated with a feeling of oppression about an hour after eating. These symptoms were never considered alarming by the patient, nor did they give him any marked discomfort, and were generally relieved by some simple remedy. For the past week they have become more severe, the nausea and vomiting most distressing, and the bowels obstinately constipated.

The man was well developed; there was no evidence of loss of flesh, the muscles were hard and firm; the skin elastic; no jaundice; the lips and mucous membranes were of good color. The heart and lungs were normal. The abdomen was soft and natural looking, nowhere tender except along the right costal margin and epigastric regions; the patient invariably winced when pressure was made in these regions. The temperature was normal during the stay in the hospital. Urinalysis showed: specific gravity, 1024; reaction, acid; no albumin or sugar; microscopically, negative. Subsequent urinary examination was invariably negative during this first stay in the hospital. The stomach contents after a Boas test-meal showed the following: total amount withdrawn, 125 c.c.; total acidity, 32 c.c.; free hydrochloric acid, 10 c.c.; no lactic acid. Microscopically: mucus, starch granules, fat droplets, and muscle fibers.

The case was looked upon as one of indigestion with subacidity, or possibly gallstones in the gall-bladder or the cystic duct. Treatment was at once begun, the pain and nausea soon subsided, and the patient was up and about the wards in a few days feeling much benefited. On June 14, after having experienced some pain during the night, he was put to bed for examination, and the following note was made: "The patient has been doing well for the past week. This morning he complains of a continuous pain in the epigastric region, and along the right costal margin. On examination, there is to be felt in the lower epigastric region, on deep palpation, a firm, resistant mass, which can be rolled under the finger. Pressure on this mass causes the patient a distinct amount of pain; it is elongated, extending from side to side, and is apparently about the size of a fountain pen. The percussion note over it is rather dull."

The urinary examination proved negative at this time as did the stools.

Subsequent examination, when the stomach was empty, always revealed the mass. It disappeared, however, when the stomach contained food. The patient was discharged on June 22, having been in the hospital twenty days.

He was re-admitted on January 31, 1906, after an absence of seven months and eight days, complaining of "general weakness, frequency of micturition, cough, and loss in weight." He said that the great loss in his strength, and polyuria, had come on rather sud-

denly about four months previously—that is, some time in October, 1905, and that since that time the loss had been steady. A cough, which had developed a month previously, had markedly increased in frequency and violence; the expectoration, watery and thin at first, had gradually become thick and purulent. His weakness, which was steadily progressive, often compelled him to remain in bed several days at a time. Urination was very frequent, often seven or eight times during the night.

The patient's statement that he had lost 42 pounds in weight could readily be believed; there was marked evidence of loss of flesh; the lips and mucous membranes were pale, and the eyes sunken. At the apex of the right lung tubular breathing was heard as far down as the third rib, and the breath sounds were accompanied by showers of fine crackling rales; percussion over this area was distinctly dull. Hepatic flatness began at the lower margin of the seventh rib and extended to within 2 cm. of the costal margin (for the most part, the liver dulness was almost obliterated by the abdominal tympany). The abdomen was markedly distended, especially in the upper quadrants; this distention was remarkable, and was a constant feature up to the day of the patient's death, and caused marked embarrassment to respiration. The tympany over the abdomen was drum-like even in the flanks, and the superficial veins were tortuous and prominent in the upper abdomen, especially along the costal margins. On palpation, nothing of importance was to be made out, the mass which had been so easily felt during the patient's first stay in the hospital was not palpable; there were no areas of tenderness, except in the epigastrium and along the right costal margin, when the patient would wince during examination, but more, apparently, from the discomfort occasioned by pressing on a distended gut than from actual pain.

There was no ascites, and no fluctuation could be elicited anywhere. The genitals were normal, and there was no œdema nor glandular enlargement. No jaundice was ever noted (nor could any such history be obtained). The urine was clear and limpid, specific gravity 1028, acid in reaction; microscopically it contained epithelial cells, mucus, cylindroids, and an occasional pus corpuscle. There was a faint trace of albumin and a decided reaction for sugar by Fehling's test. A leukocyte count showed 15,000 per millimeter. The sputum was mucopurulent, and contained many tubercle bacilli. From January 31 to February 16 (the day of death) estimations of the total amount of urine, and the gross and microscopic appearances of the stools were carefully noted; both presented a most unusual picture, especially the stools. The total daily urinary output averaged about 4000 c.c., the maximum being in the neighborhood of 6000 c.c.; while the estimations of sugar, though varying in amounts, according to the diet, was always high. On a diet consisting of bread, meat, potatoes, etc., given ad libitum, the

total sugar output was found to be around 7 or 8 per cent. (by the polariscope); a diet as free of carbohydrates as possible, though reducing the sugar to 2 or 3 per cent., would never altogether clear it. Acetone and diacetic acid were never present, even toward the terminal stages of the disease.

The stools were, perhaps, the most remarkable feature of the condition. They were, for the most part, typical examples of pancreatic disease; they varied in amount, according to the diet and general condition of the patient. Under a full and unrestricted diet they were enormous, the total amount of fecal matter collected under these conditions in twenty-four hours was 4 liters on one occasion. The daily output, however, varied, as might be expected, according to the amount and character of food given. In appearance, they were soft or semisolid, of a leaden-brown color, while here and there scattered promiscuously about, were lumps of cheesy-looking material, yellowish-white in color, and varying in size between an English walnut and a split pea; these masses proved upon microscopic examination to be lumps of fat. Another remarkable feature was the collection of an oily viscid material, dark yellow in color, around the margin of the vessel which contained the stool. The odor was very penetrating, and was in no sense of a fecal character; it was of a distinctly rancid butter odor, and could be detected in the furthest corner of the laboratory. Microscopically, a fresh stool showed large quantities of free fat, a great amount of unaltered muscle fiber, and debris.

A chemical analysis made by Dr. C. P. Emerson showed the following: Of the total stool (dried)[1] fat, 54.6 per cent.; neutral fat, 22.5 per cent.; fatty acids, 32.1 per cent. In 5 grams (weighed after drying the evaporated stool over sulphuric acid) there was: neutral fat, 1.128 grams; split fat (fatty acids), 1.6376 grams. Microscopically, there was fat as globules and as crystals.

The urine showed Hewlett's reaction for lipase on a number of occasions in specimens rendered free of sugar; negative results were invariably obtained, however, when the reaction was looked for in sugary urine.

Our results with Schmidt's meat-test were positive. This test, it must be said, was only tried during the last two weeks of the patient's life, and when the diagnosis of pancreatic changes were certain, and when, as was afterward learned by the autopsy findings, pancreatic juice must have been entirely absent from the alimentary tract, on account of complete occlusion of the duct of Wirsung by a stone. The meat-balls, sewn in silken bags, were readily recovered in the stools between six and twelve hours after their administra-

[1] According to Emerson, Müller showed that while 84 per cent. of the fat was normally split, if the pancreatic juice be excluded, there is only about 40 per cent. This low percentage of split fat in the stool forms, according to Kinnicutt's statement, the only sure sign of absence of pancreatic juice.

tion. The outside layer of the meat-ball showed complete absence of the nuclei of meat fiber, while the inside, protected as it was from bacterial processes, showed the nuclei universally intact.

The temperature from the time of entrance of the patient to his death was elevated, running a more or less typical hectic chart. The pulse varied between 70 and 120. A summary of the clinical findings is as follows: A man approaching middle life, a well-defined history of a gradually increasing dyspepsia, with a history of a violent blow in the abdomen; the finding (seven months previous to first admission to the hospital) of a well-defined mass in the upper abdomen, corresponding in main to the clinical position of the pancreas; the sudden onset of, and gradually increasing polyuria (a symptom from which we have the right to draw the conclusion that the diabetes was more or less of sudden onset); marked loss of flesh, and a corresponding loss of strength; the development of pulmonary tuberculosis, with rapid cavity formation (about four months, according to the history), in all probability the formation of the lesion being hastened by the enormous quantities of sugar; ballooning out of the intestines; large semisolid stools, containing relatively large quantities of unaltered muscle fiber, together with superabundance of free fat, and low percentage of split fat (32.1 per cent); the presence of Hewlett's lipase reaction; and the positive results obtained from the meat-bag test of Schmidt, made a clinical picture not often seen, and one from which we drew the conclusion that we were dealing with occlusion of the duct of Wirsung, and that operative procedures might be of benefit. Unfortunately, however, the large quantities of sugar in the urine (regardless of diet), and the ever-increasing pulmonary symptoms, made the operative chances practically nothing. The patient died suddenly while walking about the ward.

Autopsy. Body emaciated. Small amount of subcutaneous fat. Heart and pericardium normal. Lungs: In the upper lobe of the right lung a large tuberculous cavity is present. The entire lung is bound down by dense pleural adhesions. The liver and kidney show some evidence of parenchymatous degeneration. The stomach and intestines are normal. The pancreas is very small and hard. Rather firmly adherent to adjacent parts. It is dense and nodular, and has a stony hardness. It is 13 cm. long and 2 cm. wide, and weighs 35 grams. The duct of Wirsung is very much dilated, and will readily admit a large lead pencil (Fig. 1). About 2 cm. from the termination of the duct there is lodged a calculus, roughly about the size of an orange seed, very irregular in outline, presenting numerous small spicules, which completely occlude the duct. When the duct is opened, about 3 c.c. of turbid fluid, which was dammed back, flows out. This fluid contains a quantity of gritty particles (sand), which are scattered throughout the duct and its tributaries. The duct of Santorini is not to

FIG. 1.—Pancreatic lithiasis, showing marked dilatation of the duct of Wirsung. *A*, stone; *B*, dilated duct.

FIG. 2.—Marked fibrosis of the pancreas.

be made out, being obliterated and enveloped in the dense connective tissue which is scattered throughout the organ and in large part replaces the gland tissue.

Anatomical Diagnosis. Tuberculosis of the lung; sclerosis of the pancreas; pancreatic calculus; parenchymatous degeneration of the liver and kidney. The microscopic examination of the organs, except the pancreas, showed nothing worthy of note.

Microscopic Examination of the Pancreas. The pancreas is almost wholly transformed into connective tissue, and presents the appearance resulting from duct obstruction (Fig. 2). The parenchyma is in great part destroyed, so that in places only islands of Langerhans persist; this point is especially well shown in the specimens. However, in places the islands seem to have been destroyed along with the parenchyma; embedded in the scar-like connective tissue, they are compressed and the nuclei are small and in places are invaded by connective tissue. Some of the islands are hypertrophied and their form altered. Areas of hyaline degeneration are not to be made out. Here and there are seen one or two small ducts, either in transverse or longitudinal section. In certain fields one sees a small patch of pancreatic tissue, the cells of the acini showing evidence of degeneration. The condition is evidently one of advanced sclerosis of the pancreas, and, indeed, the lesion is so far advanced that it is impossible to recognize it as a definite type. The connective tissue not only extends between the lobules, but also invades the acini, dividing the parenchyma into small groups of cells, such as are seen in advanced cirrhosis of the liver, to which this condition seems to be in every way analogous.

Despite numerous experiments, autopsy studies, and clinical observations, the relationship between pancreatic disease and diabetes mellitus cannot be said to be definitely established, either as to its anatomical or physiological changes. Scientific knowledge dates from the experiments of Minkowski and von Mering, who succeeded in producing permanent diabetes in dogs by total extirpation of the pancreas; they also showed if a small portion be left behind at the time of the operation, diabetes will not occur, even though this portion be separated from the duodenum and the pancreatic duct be ligated. They furthermore showed that if after extirpation of the pancreas a small piece of pancreatic tissue be inserted under the skin of the abdomen, diabetes would not occur. They, therefore, concluded that a "something" is formed in the pancreas which passes into the circulation, and brings about sugar destruction, or prevents the accumulation of sugar in the blood.

Langerhans, in 1869, described groups of cells, irregularly polygonal and having a rounded nucleus situated in the parenchyma of the lobules. These structures are termed the islands of Langerhans. Probably they have the same origin as the acini, but, according to Opie's observations, they do not communicate with the

ducts of the glands, and are independent of them; they are surrounded by a capillary network, so that their secretions may readily be taken up by the blood. Herxheimer claims to have been able by serial sections to trace definitely the transition from the islands of Langerhans to the acini, and, in contrast to Opie, claims that they are not isolated structures. These islands are three times more numerous in the tail than in the head of the pancreas, and doubtless have some relationship imperfectly understood to carbohydrate metabolism. Læwaschew claimed he could increase their number by overstimulating the gland with repeated injections of pilocarpine, and that this increase took place at the expense of the acini; but Opie, by a series of experiments, found no such alteration taking place.

As to the function of these structures, it seems to be the accepted opinion that they are in some way associated with carbohydrate metabolism, and that diabetes is either dependent on some interference with the secretion of the pancreas, due to degeneration of these islands, or to the production of an excessive internal secretion by the islands—or, as Herxheimer states it—diabetes is due not so much to an anatomical change in the pancreas as to an alteration of the functional activity of the pancreas remaining.

The etiology of chronic interstitial pancreatitis is often obscure. It is probably a more common disease than the number of reported cases would seem to show, and many of the cases diagnosticated as cancer of the head of the pancreas are, doubtless, of this character. In 3 cases of chronic interstitial pancreatitis detected by the stony, indurated feel of the pancreas during operation for gallstones, Riedel feared malignancy, but 2 of the patients recovered and remained well for a number of years, thus disproving the idea of malignancy, and the diagnosis of the third case was confirmed at autopsy. The disease is one of the middle period of life, two-thirds of the cases occurring between forty and sixty years. One of the commonest causes is duct obstruction, due either to a pancreatic calculus in the duct of Wirsung, as in the case under consideration, to gallstones in the common duct or in the ampulla of Vater, or to neoplasms, usually malignant, obstructing the outflow of pancreatic juice. Bacteria reaching the gland, either through the duct or through the blood stream, may give rise to a chronic hyperplastic inflammation, as in the case reported by Moynihan, in which the condition followed typhoid fever and was due to the typhoid bacillus. Syphilis, tuberculosis, and alcohol may occasionally produce the condition.

As to the histological changes seen in the pancreas in diabetes, the work of Opie has cast much light. He distinguishes two forms of chronic pancreatitis: (1) Interlobular pancreatitis, characterized by proliferation of fibrous tissue between the lobules, which are invaded from the periphery, and (2) interacinar pancreatitis, in which the newly-formed fibrous tissue is more diffusely distributed within the lobules and between the individual acini. In the first type,

which follows occlusion of the pancreatic duct, the islands of Langerhans are implicated only when the sclerotic process has reached an advanced grade. In Opie's studies he noted but 1 case of duct obstruction due to calculus, with an accompanying diabetes. It was very similar to the case we report, differing, however, in the fact that the glycosuria was of mild character, the sugar disappearing when carbohydrates were withdrawn from the diet. On the other hand, in 2 of his cases with advanced sclerosis following obstruction of the pancreatic duct (1 case caused by calculi, the other by carcinoma) diabetes was absent. Hyaline transformation of the islands without any definite change in the parenchyma has also been noted by Opie.

On the other hand, several observers, notably Hanseman and Herxheimer, contend that the changes in the islands of Langerhans are of but little importance in the production of diabetes, and contend that the alteration in the parenchyma is of prime importance in the production of sugar in the urine.

As far as a study of one case permits, we are inclined to the view that sugar does not appear in the urine until the islands of Langerhans become involved in any disease of the pancreas. The clinical history of this case shows a man who has suffered from disease of the pancreas for some time. At the time of entrance into the hospital he showed evidence of this disease by the characteristic condition of his stools and the presence of a hard, nodular mass in his abdomen, which proved to be pancreas. The organ at this time was evidently markedly sclerosed and the parenchyma involved. It has been shown that the islands of Langerhans resist sclerosis following damming back of secretion upon the gland and finally suffer only when the acini are almost entirely destroyed and replaced by dense, scar-like tissue. However, at this time no sugar was present in the urine, although numerous examinations were made extending over a period of thirty days, with the patient on a full hospital diet. Seven months later, however, sugar was found in the urine and the symptoms of diabetes seemed to appear rather suddenly. From a study of the microscopic specimens, we believe that at this time the islands began to be involved in the sclerosis, and, therefore, the normal carbohydrate metabolism was disturbed.

TYPHOID FEVER IN THE AGED.

By Arthur S. Hamilton, M.D.,
of Minneapolis, Minnesota.

In the *Boston Medical and Surgical Journal* for 1842 Elisha Bartlett reported an attack of typhoid fever occurring in a woman aged sixty-three years. In commenting on this case he said: "The

principal interest of this case is connected with the age of the patient. It is now well settled that typhoid fever is, in the great majority of instances, a disease of early life. Of 138 cases, the histories of which are analyzed in Louis' *Researches*, only 10 were over thirty years old and no one was over forty. Of 147 cases cited by Chomel only 6 were over forty years old and only 1 was over fifty. The last-mentioned writer says, in his *Cliincal Lectures on Typhoid Fever*, published in 1834, that so far as was then known no case had been met with in which the patient was over fifty-five years of age. In what Osler[1] describes as the first articles ever published which clearly set forth the difference between typhoid and typhus fevers, Gerhard, of Philadelphia, had said that the age of those affected with typhoid rarely exceeded thirty years. With these opinions Bartlett did not wholly concur, and, in the course of his article, he stated that he believed this disorder to be of more frequent occurrence in those of advanced years than was generally held to be the case. He thought that the susceptibility to the disease, in an unprotected person, did not diminish with increasing age and believed that its comparative infrequency in advanced years was due to the fact that so many had suffered from it in an earlier period of life, it being then thought that no one could contract typhoid fever the second time. This opinion of Bartlett, however, would seem not to have been generally accepted, for, several years later, George B. Wood,[2] in speaking of typhoid fever, said: "It is comparatively rare beyond thirty years, much more so beyond forty, and very rare indeed beyond fifty." Since Wood's time, however, a number of articles have appeared calling attention to the relation between old age and typhoid fever, and, even previous to the appearance of Bartlett's article, Prus[3] had reported an attack in a woman of seventy-eight. In 1859 Uhle[4] contributed a lengthy article on typhoid fever in old people, and in 1888 Lautre[5] published a similar article. In February, 1898, Morris Manges[6] called attention to the matter and reported 5 cases in individuals past sixty, all coming under his observation during the year 1897. He thinks that the disease is not infrequent in the aged, and that its presence is often overlooked. Most authorities, however, still consider typhoid as occurring very rarely in old people, and the general opinion is that it is rarely seen. The number of isolated cases on record, depending for their interest on the age of the patient, would seem to indicate this. Osler[7] states that of 829 cases admitted into the Johns Hopkins Hospital up to May 15, 1899, there were 6 between fifty

[1] A Text-book of the Practice of Medicine, p. 2.
[2] Practice of Medicine, 5th ed., i, 351.
[3] Rev. méd. franç. et étrang., Paris, 1837, i, 62.
[4] Arch. f. physiol. Heilk., Stuttg., 1859, N. F., iii, 76
[5] Rev. méd. de Toulouse, 1888, xxii, 245.
[6] Med. Record, February 26, 1898.
[7] Johns Hopkins Hosp. Reports, viii, 421.

and sixty and 6 above sixty. He agrees with Manges that, as the course of the disease is often atypical, the diagnosis will be uncertain, and, in this way, cases will be overlooked In 2 of his cases the disease was not recognized until the autopsy was made. In the article mentioned above, Manges quotes from the statistics of the New York Board of Health, and says that out of a total of 3634 deaths from typhoid fever, occurring in that city from 1887 to 1896 inclusive, 96, or 2.6 per cent., were in persons over sixty-five, and 414, or 11.3 per cent., were in persons between forty-five and sixty-five. Even allowing for the high death rate in the aged, this evidently means a considerably higher percentage of typhoid fever in old people than is ordinarily derived from general hospital statistics.

In continuation of the work of Manges, I have collected statistics of the Health Departments of Chicago, Boston, and St. Louis, kindly placed at my disposal by the city physicians. The results are similar to those reported by Manges.

TABLE I.—*Department of Health, Chicago.*

Year.	Deaths all ages.	Over fifty years of age.
1897	437	56
1898	636	47
1899	442	57
1900	337	37
1901	509	48

TABLE II.—*Department of Health, Boston.*

Year.	Deaths all ages.	Over fifty years of age.
1897	173	34
1898	185	20
1899	165	12
1900	143	8
1901	142	9

TABLE III.—*Department of Health, St. Louis.*

Year.	Deaths all ages.	Over fifty years of age.
1897	124	6
1898	95	6
1899	131	3
1900	168	16
1901	198	10

Total number of deaths, all ages, 3885. Total number over fifty years, 369. Percentage of cases over fifty years, 9.5.

In an epidemic of typhoid fever which occurred at the Hospital for the Insane at Independence, Iowa, a number of people quite well advanced in years contracted the disease, and a study of the statistics of these cases leads me to believe with Manges and others that those in middle and advanced life are much more likely to be

attacked than is usually conceded to be the case. Out of a total of 188 cases of typhoid fever studied at the Independence Hospital, 27, or 14.3 per cent., were in individuals fifty years of age or over.

TABLE IV.

Ages.	Cases.	Actual ages.
50 to 54	6	50, 51, 51, 52, 53, 53.
55 to 59	8	56, 56, 57, 57, 58, 58, 59, 59.
60 to 64	9	60, 60, 60, 61, 61, 61, 61, 63, 63.
65 to 69	1	65.
70 to 74	2	71, 71.
75 to 79	1	78.

The mere fact that in so large a percentage of these cases the individuals were well advanced in years, however, cannot be taken as of much value in determining the liability of aged people to contract typhoid fever, since there were very few in the hospital below twenty years of age, and the presence of young people in the proportions in which they are found in general medical work would undoubtedly lessen very considerably the relative number of old people who became ill, so that these statistics cannot with justice be compared with those of the community at large. I have, however, studied more carefully the individuals in certain parts of the hospital. For this purpose, I took those who were living in two cottages and in two wards, in all of which typhoid fever was particularly prevalent. The patients situated in this way were all on the male side of the hospital. In the above-mentioned parts of the institution there were, in all, 318 men, of whom 65, or 20.44 per cent., contracted typhoid fever. So far as known, there was nothing in the surroundings or condition of these 65 patients which would render them any more susceptible than the others. Below is a table showing the number and percentage of those who, at these ages, developed typhoid fever.

TABLE V.

Ages.	Cases.	Those who developed typhoid.
20 to 29	55	15 or 27.27 per cent.
30 to 39	89	24 or 26.96 "
40 to 49	78	17 or 21.79 "
50 to 59	44	5 or 11.36 "
60 to 69	41	2 or 4.87 "
70 to 79	8	2 or 25.00 "
80 to 89	3	0 or 0.00 "

Average age of all, 43.13 years.
Average age of those who contracted typhoid, 38.9 years.

The small number of cases considered makes it impossible to draw any very positive conclusions from these statistics. Yet, in so far as they can be relied upon, they would seem to show that the liability to typhoid fever is very little less from thirty to forty than it is from twenty to thirty, and that the liability from forty to sixty is altogether beyond what one would gather from most statistics.

While assuming, therefore, that there may be considerable error involved in these figures, I am still of the opinion that the immunity to typhoid fever conferred by advancing age is less than is generally supposed, and I believe that statistics gathered from patients in private life would produce somewhat different results from those which we now have, which are almost invariably taken from general hospitals, where, as Curschman[8] states and shows by statistics, the class of patients received does not represent the average population of a community, since young or middle-aged unmarried people are much more likely to be admitted than older people.

In considering the clinical course of these cases, my attention has been drawn to a number of points in which the symptomatology has differed from that of the classical form of typhoid fever as observed in younger people. Not all of the 27 cases ran this atypical course, yet marked variations were common. In 3 cases, at least, the degree of aberration was so great that they would not have been included in the list of typhoid patients had not the subsequent development of a Widal reaction, not present at the outset, made positive the diagnosis. All the cases, however, differed widely from one another, so that it would be very difficult, indeed, to construct a type case of typhoid fever for an old person. In a general way, it may be said that the signs in the aged differ from those of younger people in that those on which we ordinarily depend largely for diagnosis, namely, a certain type of fever, rose spots, enlargement of the spleen, and nose-bleed, are frequently absent; whereas, the various complications which, at times, are so misleading in diagnosis, are likely to be present to a marked degree.[9]

Inasmuch as the patients whom I had to study were chiefly cases of senile dementia, or of terminal dementia of a high grade, it was difficult to elicit fully the subjective signs of the onset of the attack. Yet from the information at my command, I am inclined to believe that the prodromal period is lengthened, though the headache, nose-bleed, general malaise, chilly sensations, and pains in the back and legs, so prominent in younger people, are usually present in mild form or else are largely absent; thus, nose-bleed during the prodromal period, was not noticed in any case. In two instances, altogether unusual premonitory symptoms were present. In a man of fifty-eight, not an epileptic, the first thing noticed was an epileptiform convulsion. No diagnosis was made in his case until a Widal reaction was sought for and obtained, one week later. A woman of fifty-nine presented at the outset typical signs of uremia, except that she had a temperature of 103°, and the urine gave a diazo reaction. Several days later a Widal reaction was obtained in her case also.

[8] Nothnagel's Encyclopedia, Typhoid and Typhus Fevers, pp. 56, 59.

[9] It is proper to state that Curschman considers complications in this class of cases relatively infrequent, and Lautre says that they generally do not occur; but this is quite contrary to the ideas of others who have contributed to the subject and to my own experience.

During the attack that followed there was but little in her symptoms that pointed to typhoid fever, though two well-marked subsequent relapses were quite typical; throughout her illness, however, the signs of renal involvement continued very prominent.

When the disease had become fully established, the temperature curves rarely conformed to the classical type. In only 1 of the 27 cases was there any marked tendency to the production of this well-known curve. The ordinary diurnal variation is, in old people, much increased, and in almost every one of the 27 cases the temperature was distinctly remittent, even from the onset conforming closely to Strümpell's period of steep curves. In 7 cases it was even intermittent, reaching the normal two or three times during the first week.

In 5 cases the highest temperature recorded was between 105° and 105.8°. In 15 cases it was between 104° and 105°; in 5 cases, between 103° and 104°; and in 1 it was 102.6°. The average temperature in these cases, however, was by no means so high as this. As a usual thing it did not go above 102° or 103°, and in a few cases it was even lower. Along with a low grade of febrile movement it was noticed that the period of lysis came unusually early. Defervescence usually began so soon that by the eighth to the eleventh day the temperature would be normal or practically so, yet it would rarely remain there, and a marked tendency to great prolongation of slight febrile movement was observed. In only 3 cases did the temperature remain substantially normal after the first reaching that point. In 7 cases after reaching normal, there were rather slight variations extending over a considerable period, and in 11 cases there were one or more distinct recrudescences in addition to these slight variations. Of the latter, 1 case underwent also two distinct relapses, and 2 cases had one relapse each; the remaining 6 terminated fatally. Curschman refers to this irregularity of the temperature, and says:[10] "Not a few cases pursue so anomalous a course that the form of the curve furnishes no diagnostic information whatever, but rather may lead to incorrect conclusions." He also states, however, that the frequency of relapses and recrudescences diminishes distinctly with increasing years—a finding quite at variance with mine. Osler [11] reports a case with several normal or subnormal temperature records during the early part of the disease, and almost every writer on the subject refers to the striking irregularity of the temperature.

Chills and sweats seemed also to be more common in the aged than in younger individuals. In 6 of my cases there were well-marked rigors during the course of the disorder, all accompanied by profuse perspiration, and in 1 other case there was profuse perspiration without rigor. These were not mere chilly sensations, and were not produced by the baths. In a case complicated by menin-

[10] Nothnagel's Encyclopedia, Typhoid and Typhus Fevers, p. 341.
[11] Johns Hopkins Hosp. Reports, iv, 29.

gitis, to be described later, chills and sweats were very pronounced. At the same time there was very great irregularity in the fever, the rectal temperature at one time during the height of the disorder being only 95.6°. On the evening of the same day it was 104.6°, a rise of 9° in twelve hours.

Functional disturbances of the circulation were also very common, and in 70 per cent. of the cases the pulse was described as bad at some time during the disorder. In 39 per cent. of the cases there was distinct intermission of the pulse. Even in those individuals in whom the general manifestations of the disorder were quite mild the pulse, though strong and regular at the outset, would fall after a couple of weeks out of all proportion to the severity of the general symptoms, and it was also noticeable in a number of individuals that the pulse did not return to the normal for some time after the fever had subsided and the patient seemed to be doing nicely in other respects. Two patients had a mitral systolic murmur and one had an aortic systolic murmur. These were, doubtless, all organic in origin. A fourth patient had an aneurysm of the right common carotid. In 1 individual of fifty-nine there was a very high grade of arteriosclerosis, the radial arteries being typically beaded. The pulse in this patient was very intermittent throughout the attack and, on several occasions, almost imperceptible. In spite of two well-marked syncopal attacks, the patient recovered, and is now in fair health. Another man had phlebitis of the left saphenous and left external and common iliac veins, and died on the twenty-seventh day. A marked slowing of the pulse during convalescence is reported as common by some writers, but it was observed in only 2 of my cases, and even then the pulse did not go below 50.

The Widal reaction was present in every case, but as the examination was made merely for its scientific interest in most instances, and as the tests were carried out only as time permitted, I can say nothing as to the period of the disease at which the reaction first appeared.

Disturbances of the respiratory system, in my cases, were quite as common as those of the circulation, though Lautre says that usually only bronchitis or slight congestion is observed. Cough was present in about 90 per cent. of the cases, and rales were observed a number of times, but these were not studied with sufficient care to enable me to gather percentages. Pneumonia was present as a complication four times, once at the outset of the fever and three times during convalescence. In 1 of these cases pleurisy was severe, and in another case pleurisy was present without signs of pneumonic invasion. In two individuals who died, small tuberculous foci were found postmortem, but these doubtless exercised no influence on the course of the disease. Epistaxis was not common, being present in only 12 per cent. of the cases. The infrequency of epistaxis in old people has been noticed by other observers.

Marked disturbances of the alimentary tract, though less common than those of the lungs, were still frequent and severe. The appearance of the tongue did not differ from that ordinarily seen, except that it seemed a little more tremulous, more deeply furrowed, and more often dry. Eleven out of 27 vomited more or less at some time during their illness, and some to a very marked degree. Two, on account of their mental condition, refused absolutely to take any food or medicine, and had to be fed by the tube. After the third feeding one of these began vomiting, and continued so throughout, vomiting everything put into his stomach. He was next fed by the rectum for a couple of days, but his rectum soon became so irritable that it also rejected everything put into it, and in a short time the man died from combined inanition and organic heart-failure. This man was seventy-eight years of age, the oldest of the series. The other man who had to be fed with a tube began to take milk by mouth after a time, but eventually developed pneumonia and died on the thirty-first day. During the last five days he had severe hiccoughs, which continued, at times, for as long as six hours without interruption. He was seventy years of age.

During the prodromal period of the disorder constipation was more frequent than diarrhœa, 71.4 per cent. being classed as constipated; but, as soon as the disease was well established, diarrhœa became very common. Dreschfeld[12] says diarrhœa is frequent, but not usually profuse. Wilson,[13] Hutchinson,[14] and Murchison[15] think it less common than in younger people. Josias[16] and Lautre say it is always present and Curschman[17] thinks there is no difference between old and young in this respect. In 11 of my cases diarrhœa was present throughout the attack. In 7 it was present nearly all the time. In 3 cases there was persistent constipation, in 3 others the patient alternated between constipation and diarrhœa, and of 3 there is no record. The stools in the cases of diarrhœa were often of a peculiarly fœtid character.

In 18 cases tympanitis was quite marked, and in one instance the distention was very great. The unusual number of individuals who suffered from abdominal distention is probably accounted for by the general flabby condition of the tissue of old people, as well as by the intestinal disturbance. Hemorrhage from the bowels occurred three times, in 1 patient once, in another patient three times, and in a third patient four times, in the last instance resulting in death. Perforation, with subsequent peritonitis, was present but once. This case also terminated fatally. Enlargement of the spleen is said by some authors to be quite uncommon among old people affected with typhoid fever, yet in our cases it was made out in about 40 per cent., and the post-

[12] Allbutt's System of Med., p. 834.
[13] Amer. System of Practical Med., i, 203.
[14] Pepper's System of Med., i, 242.
[15] Quoted from Lautre, Ibid.
[16] Thèse de Paris, 1881.
[17] Nothnagel's Encyc., p. 342.

mortem examinations in the 6 cases which came to autopsy bore out this finding. In 2 of the 6 cases the spleen was very small, in 2 it was slightly enlarged, and once it was very large, weighing 715 grams. In the 27 cases reported herewith, jaundice was present three times. All 3 patients showed symptoms of cholecystitis, from which all recovered without operation. As 3 other cases of jaundice occurred during this epidemic, all in patients a little below fifty, and, as Osler says, that out of the first 500 cases of typhoid admitted to Johns Hopkins Hospital there was no case of jaundice, the presumption seems a fair one that infections of the biliary apparatus are more common in the aged than in the young, though a study of Camac's[18] and Keen's[19] statistics fails to bear this out.

As might be expected, disturbances of the genito-urinary system were also frequent. The diazo reaction was obtained 16 times and 6 times it was absent. In the 6 cases repeated examinations were made, so that it can be definitely stated that no reaction was present. In 5 cases there is no record of any adequate examination. In 22 cases in which the test for albumin was made it was found present every time, 13 times in considerable or large quantities and 3 times in small amount. In 5 cases there is no record of any adequate examination. Casts were found 14 times, and were positively excluded 8 times. In one instance hyaline casts only were found; in all the others pale and dark granular casts also were observed. In a considerable number of cases there was retention of urine, requiring catheterization, and, probably partly in consequence of this, pus in considerable amount was found in the urine of a good many patients, though this was present several times when no catheter had been used. Curschman[20] thinks that febrile albuminuria occurs with the same frequency as at the other periods of life, and that typhoid nephritis is met with much less often in old people.

In the seventy-eight-year-old patient who died from inanition and heart trouble, bilateral orchitis developed early in the disease. It had begun to improve somewhat at the time of his death. In a case mentioned at the beginning of the paper, the symptoms of renal disturbance were marked throughout. When first noticed, the patient was very pale and showed moderate œdema, which rapidly increased. There was total suppression of urine for a time, and what was passed subsequently contained a considerable number of casts and a moderate amount of albumin. The œdema persisted throughout the attack, which lasted, with two relapses, 124 days. A peculiar feature in this case was that the diazo reaction persisted after the temperature had fallen below 101°, something which I have not seen present in any other case.

[18] Johns Hopkins Hosp. Reports, viii, 339.
[19] Surgical Complications and Sequelæ of Typhoid Fever, p. 263.
[20] Nothnagel's Encyclopedia, Typhoid and Typhus Fever, p. 343.

Notwithstanding the already disturbed mental state of these patients, symptoms connected with the nervous system were not common. In 3 there was mild delirium and 3 were quite stuporous. Several were quite restless and were with much difficulty kept in bed, but this was probably not much more noticeable than would have been the case had the same individuals been confined to bed from any other cause. In a few cases there was a very striking mental improvement following the onset of the fever. General tremors were very common, as might be expected. As already mentioned, in 1 instance the illness was first noticed after an epileptiform convulsion. This man was probably well along in the first week of the attack. One patient, with true typhoid meningitis, presented marked mental symptoms. Throughout her attack she was very restless and emotional, and there was a pronounced general tremor. Her pupils were very sluggish and at the last were firmly contracted. Cultures made immediately after death from the brain cortex of this woman revealed pure typhoid bacilli, and, later, bacilli resembling typhoid germs were found in the brain tissue itself.

It seems to be quite generally accepted that rose spots are less common in old people than in the young, and in this series they were present only five times, twice in large numbers, and three times in small numbers. One patient presented quite large patches of erythema, which were present only two days.

Convalescence was an exceedingly tedious process, for, as already mentioned, when the temperature had about reached normal it would still persist in slight elevations, sometimes for many days. In those cases especially in which the attack had been severe the patient was left very weak and considerably emaciated. In such individuals, when lying in bed, disturbances of the lungs, which delayed the period of convalescence, developed several times. One patient who had seemed to be convalescing fairly well, though still very weak and lying helplessly in bed, suddenly developed pneumonia and died. Two cases were much delayed in convalescence by attacks of cholecystitis. Setting the limit of recovery at the time when the patient was able to be dressed and walk about, the longest illness was 124 days. This was in the woman who presented symptoms of uremia and who had two relapses. The next longest illness was 120 days, and was in one of the women who developed cholecystitis during her convalescence. The shortest illness was 26 days, and the average about 60 days. It has been said by some that marked subnormal temperatures are characteristic of the period of convalescence, but this has not been my experience. In 3 cases the temperature was between 95° and 96°, but in most instances it usually did not go below normal. There was a very close relationship between the feeding of the patient and the development of these subnormal temperatures. Those who were kept long

on liquid diet became very weak and their temperatures showed a decided tendency to become subnormal. Those who were given more solid food at an early stage showed but little such tendency.

As will be seen in the foregoing study of the symptoms, diagnosis is by no means easy, and there is a rather extraordinary variation in the symptoms as described by different men. The temperature curve is more often misleading than otherwise. Enlargement of the spleen, rose spots, and nose-bleed are also often absent. The presence of diarrhœa, with a peculiarly offensive odor, may be of some value when associated with other symptoms, and Lautre says it is absolutely diagnostic, yet it may, of course, be present in many other conditions. The diazo reaction in the cases presented here proved to be of no great value. Its frequent absence and the fact that it may be due to so many conditions other than typhoid fever make it of little use. The one sign which was altogether satisfactory was the Widal reaction. Without it, I feel sure that many cases of typhoid fever in old people must pass under other names.

As one would expect, the death rate is much higher than in younger individuals. Murchison in a series of collected cases found a mortality of 34.94 per cent. Of my 27 patients 6 died, making a mortality of 22.22 per cent. The causes of death were as follows: Intestinal hemorrhage, perforation and peritonitis, inanition and organic heart disease, phlebitis, pneumonia, and typhoid meningitis.

For lack of time I will say nothing of the postmortem findings, except that they conformed quite closely to the conditions found in younger people, with this addition, that many of the organs showed chronic disturbances as well as acute pathological conditions.

The treatment in most respects was such as would have been employed in younger individuals, with special watchfulness for cardiac, pulmonary, and genito-urinary complications. In the milder cases very little is needed to combat the fever, as it seldom rises high. Two of my patients had no treatment at all for this condition. For the more serious cases bathing of some sort was necessary. In some cases tub baths were borne quite as well as in younger people, but in a number of instances the patients shivered so excessively after the bath and became so cyanotic that we did not employ it at all in 7 instances, using sponge baths instead; six patients began with tub baths, but were treated later with sponge baths only, and 12 patients had tub baths exclusively. For the diarrhœa intestinal astringents and antiseptics were found beneficial, and for the bladder disturbances urotropin was unusually satisfactory. In those whose bladders were healthy at the onset of the disease, 7 grains of urotropin every four hours or at less frequent intervals almost invariably produced a favorable result in two to four days. In those who had chronic bladder troubles the results were less satisfactory. To prevent pulmonary complications during convalescence, I think

it advisable to have the patient sit up in bed as soon as possible, and as already stated, something more than liquid diet should be given as soon as the fever has subsided to near normal. The dangers in old people of an exhausted condition with prolonged convalescence are, in my opinion, greater than are those of relapse and perforation from too early feeding.

ATROPHY OF THE PARATHYROID GLANDULES AND OTHER GLANDULAR STRUCTURES IN PRIMARY INFANTILE ATROPHY.

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My purpose herewith is to emphasize the constant finding of atrophy of the thymus gland in infantile atrophy, and to report a particular case in which there was marked glandular atrophy not limited to the thymus; but more especially I desire to call attention to the condition of the parathyroid glandules in infantile atrophy, to which, up to the present time, scant attention has been paid.

That certain glands are involved in disturbances of nutrition was pointed out as early as 1858 by Friedlieben,[1] who stated that the size and condition of the thymus was an index to the state of nutrition of the body. This observation has been confirmed by a number of investigators, among the more recent of whom may be mentioned Mettenheimer,[2] Stokes, Ruhräh, and Rohrer,[3] and Dudgeon.[4] The main conclusion of these authors may be summarized in the statement that atrophy of the thymus gland in children and wasting of the tissues go hand in hand. Dudgeon states, moreover, that atrophy of the thymus gland is the most characteristic morbid lesion found in cases of marasmus.

The average weight of the thymus at birth, as given by different authors, is at great variance, as will be seen from the following series of weights given in different text-books: Testut (Quain's *Anatomy*), 5 grams; Robinson (Morris' *Anatomy*), 14 to 28.5 grams; Vierordt (Hektoen's *Pathology*), 24 grams; Howden (Gray's *Anatomy*), 15 grams; Osler (*Practice of Medicine*), 14 grams; (second year, 25.30 grams); Ziegler (*Text-book of Pathology*), 24 grams; Roberts (Albutt's *System of Medicine*), 15 grams; Fowler (*Encyclopedia Medica*), 15 to 30 grams; Friedlieben, 13.7 grams;

[1] Die Phys. der Thymusdrüse in Gesundh. u. Krankheit, Frankfurt, 1858. Ref. Dudgeon (loc. cit.).

[2] Jahrb. f. Kinderheilk., 1897, lxvi, 55.

[3] Amer. Jour. Med. Sci., 1902, cxxiv, 847.

[4] Jour. Path. and Bact., 1905, x, 173.

two years, 26.2 grams. It appears that most writers have agreed with Friedlieben, and quite recently Hammer[5] gives the weight of the thymus at birth as 13.26 grams; and from the first to the fifth year, 22.98 grams. On the other hand, Thursfield[6] finds the average weight 6 to 7 grams, Dudgeon gives the weight as 7 to 10 grams, and Bovaird and Nicoll,[7] who recently reported on some 600 autopsies, give the average weight as 7 grams. In 25 cases, from birth to one year of age, excluding marasmus, I have found the average weight of the thymus to be 7.25 grams.

It seems to be a commonly accepted idea that the growth of the thymus gland proceeds during the first two years of life, and from that time remains somewhat stationary (although the parenchyma is replaced more or less by connective tissue) until puberty, when atrophy becomes rapid. Remnants of the gland can be found, however, in most instances in adults, even in advanced age. Hammer finds constant increase in weight up to puberty. Boviard and Nicoll state that the thymus does not increase in weight after birth; that there is no evidence of growth, although under certain conditions the gland may undergo hypertrophy. I am inclined to agree with them, and I have found no evidence to support the commonly accepted idea of growth of the gland up to two years of age. On the contrary, evidences of atrophy can frequently be found from birth, although these atrophic changes are not of necessity accompanied by loss of weight.

While a direct ratio has been noted between atrophy of the thymus gland and wasting diseases in children since the time of Friedlieben, as stated above, it is more recently that attention has been drawn to the fact that the most characteristic and constant lesion of the so-called primary atrophy in children, or marasmus, aside from atrophy of fat and muscle, is atrophy of the thymus gland. Marasmus, as defined by Morse,[8] "is a morbid condition of infancy in which there is extreme wasting of the soft tissues of the body without demonstrable organic lesions. It is the expression of continuous insufficient nutrition, due probably to defective absorption or assimilation rather than to defective digestion." Parrot[9] first described the disease in 1877 under the name "athrepsia," and considered it an acute starvation. Babinsky[10] found a chronic intestinal catarrh in his cases, with extensive atrophy of the intestinal wall, and concluded that "marasmic atrophy of the intestine caused death by starvation." This author also found that 37.1 per cent. of nutritive substances were unassimilated in this disease and passed in the feces. Bendix,[11] however, found Babinsky's nitrogen esti-

[5] Arch. f. Anat. u. Phys. Jahrg., 1906, Anat. Abt., Sup. Band, S. 91.
[6] St. Barth. Hosp. Rep., London, 1903, xxxviii, 129.
[7] Arch. of Pediat., September, 1906.
[8] Med. News, 1901, lxxix, 409.
[9] Progres medicale, 1874-5.
[10] Brit. Med. Jour., 1899, 1084.
[11] Jahrbuch f. Kinderheilk., 1896, Band lxiii.

mate exaggerated. Fenwick[12] found inflammatory changes in the mucosa of the stomach and intestines in 16 cases, and called attention to the lack of HCl in this condition. Heubner and Rubner[13] concluded that the disease is due to auto-intoxication from decomposed food in the intestinal tract, and Marfan[14] claimed a lessened activity of nutritive ferments to be the main cause of the condition. Symes[15] considered that "improper food induced disorganization and morbid secretion of the digestive glands."

None of these statements has lead to definite conclusions, however. Holt[16] does not consider the intestinal lesions described by other investigators as of importance in the etiology of the disease, and Wentworth[17] states that metabolism observations in infantile atrophy have shown a diminished power of absorption by the intestine for artificial foods, but they do not explain the cause of this failure to absorb, and he believes that the cause of infantile atrophy cannot be discovered by metabolism investigations.

Whatever the cause of the disease may be, the autopsy findings in this condition are unsatisfactory, and there is no lesion that is specific. At the postmortem, marked wasting of fat and muscle is noted; the heart, kidneys, and liver may show fat; the mucous and submucous coats of the stomach and intestines may show atrophy; the lymph nodes may be enlarged. Death may be due to a terminal infection, such as bronchopneumonia or enteritis. As has recently been emphasized, in addition to these findings there is present notable atrophy of the thymus gland, which is not specific for primary atrophy, but is found in other wasting diseases of infants.

Stokes, Ruhräh, and Rohrer examined 18 cases of marasmus and found the average weight of the thymus for 16 of the cases to be 2.2 grams. The smallest weighed 1.2 grams, and the largest weighed 7.5 grams. Dudgeon examined 15 cases and found the average weight 2.68 grams. The smallest weighed 0.905 grams and the largest, 5 grams.

I have had the opportunity to examine the thymus in 20 cases of marasmus at autopsies at St. Ann's Asylum, in infants from birth to one year of age. In every case I have found a notable atrophy of the thymus gland. The smallest weighed 1 gram (2 cases); the largest weighed 4.75 grams. The average weight of the gland was 2.472 grams. This result was practically the same as that of Stokes and of Dudgeon.

Little can be added to the histology of these glands as described by the aforesaid authors. I have found Mallory's phosphotungstic acid-hematoxylin stain the most satisfactory for their routine stain-

[12] Brit. Med. Jour., 1896, ii, 829.
[13] Zeit. f. Biologie, 1899, Band xxxviii.
[14] Rev. mensuelle des mal. de l'enfance, 1901, tome xix.
[15] Brit. Jour. Chil. Dis., 1906, iii, 290.
[16] Diseases of Infancy and Childhood, 3d ed., 1907, 240.
[17] Jour. Amer Med. Assoc., 1905, xlv, 771.

ing. With this stain the connective tissue is clearly differentiated, the cell nuclei are sharply defined, Hassal's corpuscles are prominently shown, degenerative products such as droplets of hyaline are distinct, and fibrin threads, or masses, which are frequently found in the bloodvessels, are beautifully demonstrated.

In general it may be said that in most instances all differentiation between cortex and medulla of the gland is lost. The replacement of lymphoid cells by cells which are evidently of connective-tissue or endothelial origin, as observed by Dudgeon, is frequently found. There is always a marked increase of connective tissue in the gland which divides it into numerous small lobules, some of which may be further invaded by connective tissue replacing the parenchyma. Hassal's corpuscles are rendered prominent by atrophy of the contiguous tissue, and present a variety of degenerative changes. The walls of the bloodvessels may be thickened. The vessels may contain fibrin thrombi.

It may be said in summarizing these cases that all infants dying of marasmus exhibit marked atrophic changes of the thymus gland.

While the thymus gland occupies a somewhat anomalous position in respect to other glands, nevertheless it cannot be wholly separated from, and usually is connected with, that group of structures that have to do with internal secretion, and are known as the "ductless glands." The structures included under this title of "ductless glands" are, at the present time, according to Vincent, the thyroid, parathyroids, cortical and medullary suprarenal, pituitary, the carotid and coccygeal bodies, and possibly the thymus.

In consideration of the physiological relationship between the thymus and these other structures, the following case[18] is of interest in showing that glandular atrophy is not always limited to the thymus in these cases of infantile atrophy, but may be exhibited in other glands of this group. In this instance, in addition to changes in the thymus, extreme atrophy was found in the thyroid, parathyroids, and medullary suprarenals.

This infant was admitted to St. Ann's Asylum when nine days old, and was in good condition. There were no errors of development. The weight was 9 pounds, 5 ounces. The infant progressively lost in weight, although at times there was a slight gain in weight which was never permanent. When the infant was seven months old it weighed 3 ounces less than when admitted. At this time physical examination showed the lungs clear, and the heart normal. It presented the typical picture of marasmus. During the next three months there was some improvement. At the eleventh month the infant weighed 10 pounds, 5 ounces. Then diarrhœa and vomiting developed and death ensued.

The autopsy protocol is, in brief, as follows: Weight, 10 pounds;

[18] I wish to express my indebtedness to Dr. J. M. Brady for supplying me with the clinical notes on this case.

body is much emaciated; lividity of dependant parts; typical marasmus facies; no "rosary" or other evidence of rachitis; skin dry; muscles pale and atrophic; abdominal cavity normal; intestines somewhat distended; no mesenteric, abdominal, or retroperitoneal fat; appendix normal; mesenteric lymph nodes not enlarged; pleural cavities and pericardial cavity normal. Heart normal in size; epicardium, myocardium, and valves normal; foramen ovale, patent 2 mm. Lungs: upper lobes pinkish-gray in color; air containing throughout; normal on section. Lower lobes, dark red in color; firm, and present areas of solidification, especially in posterior part. On section color dark red, with irregular grayish, granular, slightly elevated areas throughout. Bronchi contain mucus, streaked with purulent material. Spleen normal in size, dark red in color, consistence fairly firm; normal markings are seen on section. Stomach, intestines, and pancreas normal. Liver slightly smaller than usual; color dark reddish-brown, consistence normal, markings normal on section. Gall-bladder and ducts normal. Gall-bladder filled with thin pale fluid. Kidneys normal in size, capsule strips easily leaving a smooth surface. Organs appear normal on section. Suprarenal glands, very pale grayish-white in color; the left measures 3 cm. long by 1 to 2 cm. wide, by 0.5 to 0.7 cm. thick. On section, cortical portion appears as dirty gray zone; medulla is brown. Right adrenal, 2.5 cm. long by 1 cm. wide, is very thin (1 mm.) and presents on section no color differentiation. Genito-urinary tract normal. Organs of neck: thymus, weight 1.25 grams; measures $2.5 \times 1 \times 0.5$ cm.; has an accessory lobe $1.5 \times 1 \times 0.5$ cm. Thyroid very small and pale; lateral lobes measure 1.5 long by 1 wide by 2 to 0.5 in diameter; weight of thyroid, 1 gram. Parathyroid glandules: the upper glandules are found in normal situation; they measure 2 mm. in longest diameter; the lower bodies are not found. Head not opened.

Microscopic examination of organs:

Heart negative. *Lungs:* sections from posterior part of lower lobes show areas where the alveoli are filled with an exudate consisting chiefly of polymorphonuclear leukocytes, with a few red blood corpuscles and desquamated alveolar epithelium. The capillaries of the alveolar wall are congested and tortuous. The smaller bronchi are filled with polymorphonuclear leukocytes. The larger bloodvessels are injected. In some sections collapsed alveoli (areas of atelectasis) are seen. *Liver:* the liver parenchyma presents a normal appearance; the liver cells do not show vacuoles; capillaries show slight injection in places; periportal connective tissue normal; Scharlach R. stain shows a small amount of fat, in fine droplets, in the liver cells. Spleen negative. *Kidneys:* the tubular epithelium is somewhat swollen and glandular; the glomeruli show a slight increase of nuclei; the bloodvessels are injected; walls of the bloodvessels show slight hyaline change. *Intestine:*

thin-walled; both mucosa and submucosa show noticeable atrophy; the lymphoid tissue is prominent. *Epiphysis of rib:* shows fairly regular, even line of calcification; there seems to be a slight excess of osteoid matrix at the extreme edges.

Thymus: The entire thymus was cut in serial section and examined throughout, especially for inclusions of parathyroid tissue. None was found. In general the gland shows thick connective tissue stroma dividing the gland into small islets of lymphoid tissue, a considerable portion of which is being replaced by fatty connective tissue. Areas of focal necrosis also are seen where cells have lost their distinct outline, and a more or less homogeneous eosin staining mass results, in which swollen and fragmented nuclei can be seen. Hassal's corpuscles are prominent; they vary in size and present granular and hyaline degenerative changes. The blood-vessels are injected, and some show hyaline thickening of the vessel wall.

Left Suprarenal: The cortical portion is of about normal thickness, and shows fairly regular zonal differentiation, and presents no change worthy of note. The medullary portion, however, is

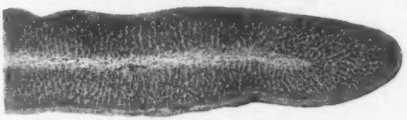

FIG. 1.—Sketch of the suprarenal body, showing replacement of medulla by connective tissue. (Magnified 60.)

much thinner than usual, and in a part of the gland is wholly absent. There is no characteristic cell grouping, but the cells are crowded together in closely-set masses, between which run irregular strands of connective tissue. The cells are swollen, the protoplasm granular or absent, and the cell boundaries not defined. In one place a zone of hemorrhage is seen between cortex and medulla.

Right Adrenal: Cortical portion similar to left adrenal. The medulla has entirely disappeared throughout and is replaced in part by a thin line of connective tissue (Fig. 1).

Thyroid: The gland shows a considerable amount of connective tissue stroma both between groups of tubules and separating the individual tubules (Fig. 2). The lining epithelium of the tubules is in great part detached from the basement membrane and the cells are heaped up irregularly, in places filling the lumina. There is no colloid present.

Parathyroid Glandules: The structure in general corresponds to the picture seen in the normal glandule. The cells form together hanging masses separated by connective-tissue stroma, bearing bloodvessels which are well injected. Within the individual masses the capillaries are found filled with blood. The "pallisade"

or "balcony" cells are not seen at the edges of the gland. There is only one type of cell to be distinguished in the parenchyma. The cell boundary, which is usually distinct, is not to be made out in general. The cytoplasm of adjacent cells is more or less fused together, and in places is absent entirely. Many of the cell nuclei are swollen and irregular (Fig. 3). These degenerative changes are evident in varying degrees everywhere throughout the glandules. Scharlach R. stain shows absence of fat.

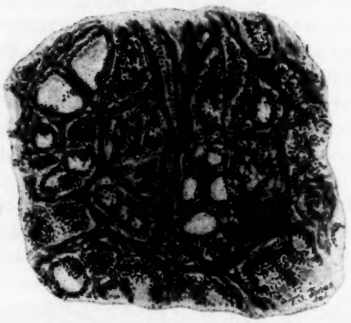

FIG. 2.—Thyroid gland, showing replacement of tubules by connective tissue and irregularity of the epithelium. (Magnified 105.)

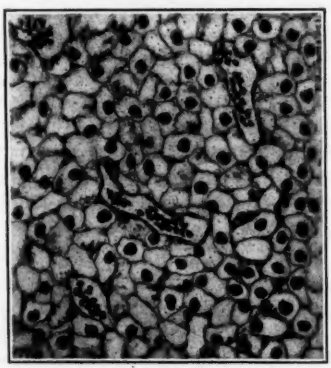

FIG. 3.—Parathyroid glandule from a case of infantile atrophy, showing degeneration of the principal cells. (Magnified 575.)

We have here, in brief, a case of infantile atrophy of one year's standing, in which the infant was kept alive for a considerably longer period of time than is usual in such cases. The immediate cause of death was a terminal infection (bronchopneumonia), which is not uncommon in these cases. The principal histological change, aside from the atrophy of fat and muscle tissue, was marked atrophy

of the medullary adrenals, thymus, thyroid, and pa athyroid glandules, which was so extreme as to attract attention macroscopically. The striking picture in this case can be accounted for, perhaps, by the long duration of the disease (one year), which lead to changes which were more marked than those usually seen in the cases, which run an average course of two or three months.

On account of the findings in this ca e it was thought desirable to see if similar atrophic changes could be found in these glands in other cases, and he following is the result of the study of the parathyroid glandules in 12 cases of infantile atrophy. (A detailed study of the thyroid, medullary suprarenals, and other glandular structures is purposely omitted in this paper.)

Parathyroid Glandules. The situation, general appearance, and microscopic structure of the parathy oid glandules of the infan do not differ essentially from that of the adult. The glandules are much smaller in the infant than in the adult. They average about 2 to 5 mm. in diam ter normally in the infant, while in the adult they average about 8 mm. in longest diameter. Sandstroem[19] gives the adult length as 2 to 15 mm. They are more difficult to find in the infant than in the adult, not only on account of their small size, but owing to their resemblance to certain lenticular bits of tissue which extend upward along the posterior border of the thyroid on both sides of the œsophagus. This tissue is continuous with the interscapular gland of Hatai,[20] and at a later period of infant life is not to be distinguished macroscopically from fat, although Warthin[21] and others consider the structure a part of the hemolymph system. Bonnot, in a paper not yet published, but to which he has kindly allowed me to refer, considers also that this structure has to do with the formation of blood in the embryo, and to some extent in the adult. In marantic infants, in whom there is no fat, this tissue persists, and the tiny nodules are extremely difficult to distinguish in size, color, and situation from the parathyroids. By preserving the neck organs entire in Pick's solution I was finally able to get a color differentiation that distinguished this tissue from the glandules. Another source of difficulty is in distinguishing the parathyroids, especially the lower, from remnants of the thymus gland which are more much frequently found in the infant than in the adult. This in many instances can only be done microscopically. Several times I have found what macroscopically I presumed to be parathyroids, to be, microscopically, parathyroid incorporated in a remnant of thymus. This is to be expected from the close embryological relationship of the two structures, and Verebely has noted the same thing in the adult.

Microscopically, certain differences between infant and adult parathyroid may be noted. The most important seems to be that

[19] Ref. Schmidt's Jahrb., 1880, clxxxvii, 114.
[20] Anat. Anzeig., xxi, 369.
[21] Amer. Jour. Anat., 1901, i, 63.

there is only a single type of cell in the infant glandule. The differentiation into "principal" and "functional" cells, as described for adult parathyroids, cannot be made. From other work on these glandules, not yet published, I had concluded that there is only one type of cell primarily in the parathyroid, corresponding to the "principal" cell, and that the so-called "functional" cell represents a modification of this cell, due either to degeneration or hyperfunction. Verebely[22] has also arrived at a similar conclusion. Fat, which is always present in the adult parathyroid, is not normally present in the infant parathyroid. Benjamins[23] has previously noted the increased amount of fat in adults as compared with the fœtus.

The following observations on the parathyroids were made in 12 cases of marasmus, in infants from birth to one year of age. To these was added 12 control cases, from routine autopsies, other than marasmus in infants of the same age.

My attention was first called to the condition of these glandules in marasmus by the greater difficulty in finding them in the marasmic than in the other cases, and estimation of the weights and measurements showed that there was a considerable difference between the two groups of cases. The average measurements of the glandules in the cases of marasmus was 2 mm. in longest diameter for the superior, and 3 mm. for the inferior bodies. This is a little more than half the average measurements of the control cases.

The literature as regards the anatomy and histology of these bodies has been so thoroughly reviewed of late that it will only be referred to casually in this place. The number and position of the glandules showed the same variation in both series that is usually found in examining adult parathyroids. The position in general showed less variation than in the adult, possibly owing to the fact that if the glandules are removed some distance from their normal situation in the infant they may not be found.

It was impossible to ob ain an exact table of the weights and measurements of these bodies, as some of the pieces that were apparently glandules macroscopically in both series proved microscopically not to be parathyroids, and deductions had to be made as nearly as possible by estimation. The estimate, which is as nearly correct as could be obtained under the conditions, showed in the 12 cases of marasmus the average weight of the four glandules to be from one-half to two-thirds the average weight of the four glandules in the cases not marasmus.

Individual glandules in the marasmus cases were found weighing as little as 0.06 gram (about a grain). None of the non-marantic cases showed such small size. In certain instances individual glandules were found in the control cases that were as small as certain of the larger glandules in the cases of marasmus.

The finding of the four parathyroids in each case in these series

[22] Virch. Arch., 1906, clxxxvii, 80.

[23] Ziegler's Beit., 1902, xxxi, 143.

less frequently than in adult cases, is accounted for by the difficulties previously mentioned and the extreme smallness of the glandules. In the 12 cases of marasmus 4 glandules were found in 6. Three were found in 5 cases. In 1 case only 2 were found. In the 12 routine cases, 4 glandules were found in 8; 3 were found in 1 case; 2 were found in 2 cases, and only one glandule in one instance.

Microscopically, the parathyriod glandules present, in the routine cases, a fairly uniform picture. They consist of closely set cell masses arranged in groups or in strands, which are separated by a rather delicate connective tissue stroma bearing bloodvessels. The relation between parenchyma and stroma is more uniform, and there is less tendency to form varying types of arrangement than in the adult. The cell masses consist of cells a little larger than

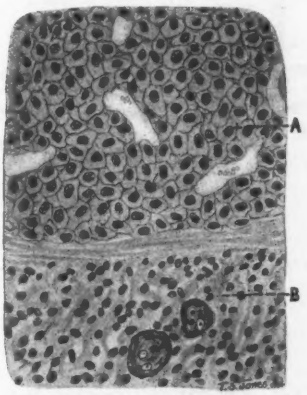

FIG. 4.—Normal infant parathyroid (*a*) in connection with (*b*) remnant of thymus gland. (Magnified 575).

those of the thyroid, which vary in size and shape and intensity of nuclear and cytoplasmic staining, but which conform to a single type, the so-called "principal" cells of the adult glandule. The cytoplasm of these cells may be indistinct or lacking, but the cell membrane is usually distinct. Along the capsule and septa these cells frequently assume a radial arrangement, the so-called "palisade" formation. As previously noted, the so-called "functional" cells of the adult do not appear in the infant gland. Not infrequently bits of thymus tissue are found in contact with the glandules (Figs. 4 and 5).

In the cases of infantile atrophy the general structure of the glandule is the same as in the other cases. The changes that are found in this condition can be quite sharply differentiated into two types, which may be designated as (*a*) degenerative, and (*b*) sclerotic.

In the first type (Fig. 3) the glandules may be diminished in size or may be of normal size, and are pale in color, or, as in 1 case that showed intense congestion, the glandules were cherry red (Fig. 6). Microscopically, no increase of connective tissue is found,

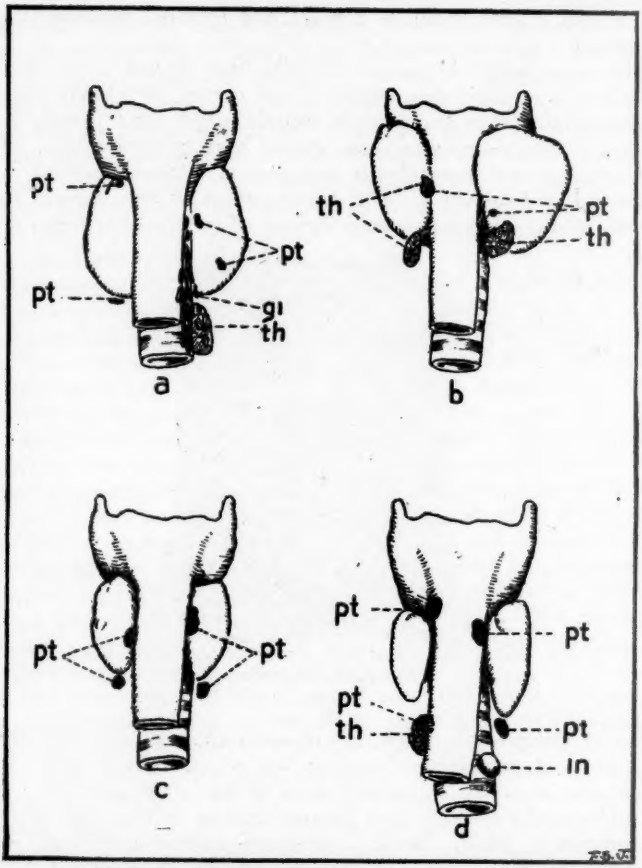

FIG. 5.—*A* and *B*. Sketch of the neck organs from cases of primary infantile atrophy, showing the small size of the parathyroid glandules; compare with *C* and *D*, which are control cases of infants of the same age. (*pt*) parathyroids, (*th*) remnants of thymus gland (in *B* replacing the two lower parathyroids and surrounding the left upper); (*gl*) represents tissue continuous with the interscapular gland. (*ln*) lymph node.

but the epithelial cells show everywhere a marked degeneration. They are larger and more irregular than normal, the nuclei are swollen and the cell boundaries are usually thickened, appearing as though the protoplasm had condensed in part at the cell peri-

phery, as happens in certain forms of reticular degeneration. In places there may be complete loss of cell structure with crowding

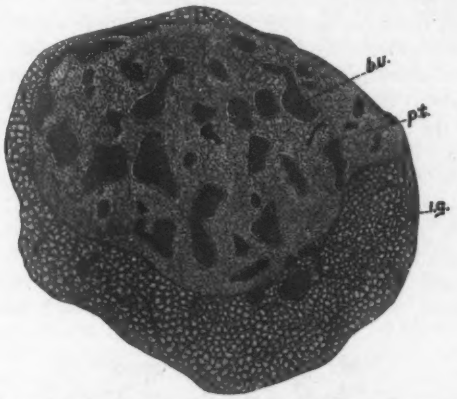

FIG. 6.—Extremely vascular parathyroid almost completely surrounded by tissue of the interscapular gland type. (Magnified 105.)

FIG. 7.—A parathyroid glandule of the sclerotic type, from a case of infantile atrophy The dark masses represent the parenchyma; the light areas the increased connective tissue. Above (*b*) is thyroid gland. Below (*c*) is a remnant of the tissue continuous with the interscapular gland. (Magnified 105.)

together of the cytoplasm into a fused mass, in which the nuclei are irregulary arranged. The bloodvessels may be greatly distended, but are usually moderately injected.

The most common finding, however, in these cases of marasmus is a marked increase in the connective tissue stroma of the glandules, which corresponds closely to the sclerosis (chronic fibrous parathyroiditis) described in the adult. These cases I have called, therefore, the sclerotic type. In these cases the glandules are smaller than normal, dark brownish-red in color, and firm. Microscopically the connective tissue stroma separating the cell masses is found increased in amount in varying degree (Fig. 7). The epithelial cells appear as irregular strands between the thickened bands of connective tissue. This connective tissue increase is frequently noted about the bloodvessels (Fig. 8). The connective tissue is loose, vascular, and rich in nuclei, which have a spindle

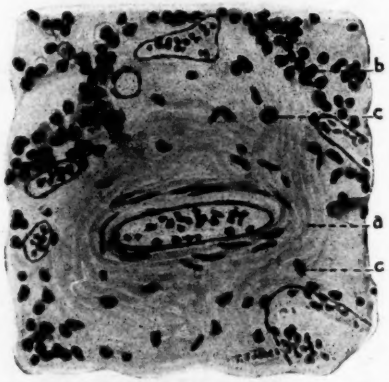

FIG. 8.—Parathyroid glandule of the sclerotic type, high power, showing (*a*) perivascular increase of connective tissue, (*b*) crowding together of epithelial cells, and (*c*) mast cells in connective tissue. (Magnified 575.)

shape. Mast cells are frequently seen in the connective tissue. In the epithelial islets between the connective tissue strands the "principal" cells are crowded together so that the typical sharp-lined epithelial structure is lost. The cell membrane is usually not seen, but masses consisting of closely set, irregularly arranged nuclei, without definite cell boundaries, are apparent. Groups of five or six cells occasionally in the centres of these islets preserve their original structure.

Briefly summarized, then, it may be stated that in primary infantile atrophy the parathyroid glandules show changes which may be degenerative in type, but which are, for the most part, progressive, and consist in replacement of a varying amount of the gland parenchyma by connective tissue stroma. These changes are similar in nature to those which are constantly present in the thymus gland

in this disease. Moreover, these progressive changes are present in other ductless glands, and become especially apparent in long-standing cases of the disease, as evidenced in the extreme atrophy of the thyroid and medullary suprarenal in the cases here described.

It is by no means my intention to imply that these various glands are primarily at fault in infantile atrophy, but rather to emphasize the fact that failures of assimilation in this disease lead to wider changes than simple wasting of fat and muscle. The fatal result in this disease is more easily understood when we realize the constant involvement of structures that elaborate substances which are so essential to health, or even life itself, as are here found.

While no definite pathology has as yet been established for the parathyroid glandules, their great importance has been shown by a long series of investigators, beginning with those of Gley.[24] In many animals the removal of these glandules results in death, with tetanic symptoms, as has been shown by Gley, Vassale and Generali,[25] Welsh,[26] and many others. All results have not been in accord, however, in the removal of these glandules in animals. The recent work of Vincent[27] and Jolly has shown that it is possible to remove both thyroids and parathyroids in certain animals without causing death.

In regard to the so-called tetania parathyroipriva that is supposed to accompany destruction of parathyroid tissue, and which is never present in infantile atrophy, the question might be asked whether such a condition might not be expected in cases in which the parathyroid glandules are involved, as here described. Vincent and Jolly, in their latest work on these glandules, are not able to confirm the theory that the removal of the parathyroids causes always severe acute nervous symptoms. They found that certain animals (rats, guinea-pigs, and badgers) did not suffer at all from their removal. Monkeys showed only transient nervous symptoms following the removal of these glandules, and nervous symptoms sometimes supervened when these bodies were left in situ after a neck operation. Therefore, we cannot consider by any means the fact wholly proved that in the human, the destruction of these bodies always induces tetany.

In the histological studies of parathyroids, MacCallum,[28] Banbrognini,[29] and Guizetti[30] have described changes in these glandules in gastric tetany, eclampsia, and traumatic tetany, respectively In general, however, the histological study of these glandules is negative in cases showing tetanic symptoms. I failed to find any

[24] Comptes rendus de la Soc. biol., 1891, p. 843.
[25] Revista di Patol. Nerv. e. Ment., 1896, i, 3 and 7.
[26] Jour. Anat. and Phys., 1898, 401.
[27] Lancet, August 11 and 18, 1906; Jour. of Phys., 1904, xxxii.
[28] Cent. f. allg. Path., 1905, 385.
[29] Ref. Cent. f. allg. Path., 1907, xxviii, 82.
[30] Cent. f. allg. Path., xviii, 81. 1907.

alteration in these bodies in 9 cases of paralysis agitans, and in an infant dying in convulsions the glandules were negative.

There remains much to be known relative to the exact nature and function of these glandules and their real importance in the body economy. It is hoped that the preceding morphological notes may be of value in stimulating study of these bodies along other lines, and that this may throw some new light on the function of these structures, especially in conditions of impaired nutrition.

A TUMOR OF THE MITRAL VALVE.

By Leonard Blumgart, M.D.,
of new york.

(From the Pathological Institute of the Kaiser Wilhelm University at Strassburg, Prof. H. Chiari, Director.)

While making an autopsy (No. III, April 2, 1907), I came upon a tumor of the left cusp of the mitral valve, which was given to me for purposes of examination.

The case was that of a woman, aged eighty-six years from the Home for the Aged. Disease of the heart was given as the cause of death. There was no clinical history.

The following are autopsy notes: A female body, 158 cm. long, well developed, and fairly well nourished. The brain is slightly œdematous, and its gyri atrophic. The lungs are œdematous, and the seat of a high grade emphysema. The trachea and bronchi show redness of their mucous membrane, which is also covered with a mucopurulent secretion. The peribronchial lymph glands are anthracotic and calcified. The kidneys are small, their capsules adherent, and the parenchyma shows degeneration. The other organs are normal, except the heart, which shows the following: (Fig. 1): The pericardium is smooth, and there is no exudate. The heart is enlarged and relaxed, weighing 495 grams. The right ventricle and right auricle are dilated, the former is slightly hypertrophied. The left ventricle is markedly hypertrophied, its wall being 2.5 cm. thick. The left auricle is also dilated. The endocardium is smooth. The myocardium shows no pathological change. The tricuspid and pulmonary valves are normal. The aortic valve is somewhat thickened, and in one place contains a calcified node. The aorta shows small areas of endarteritis deformans of a moderate degree. On the auricular side of the left or posterior cusp of the mitral valve is a tumor, $3.5 \times 2.5 \times 2$ cm. in size, irregularly round, smooth, glistening, and softly elastic. It is pedunculated, the pedicle resting on the cusp, 5 mm. from its free edge. The rest of the cusp shows several slight aneurysmatic bulgings about 0.5 cm. in depth, whose convexities are upward.

The entire heart was placed in a solution of 100 parts of alcohol, 50 per cent., and 2 parts of formalin (Museum Preparation No. 3744). After hardening, the tumor was cut as indicated by the dotted line in Fig. 1. The cut surface of the right half of the tumor is shown in Fig. 2. The cut surface is seen to be a deep homogeneous

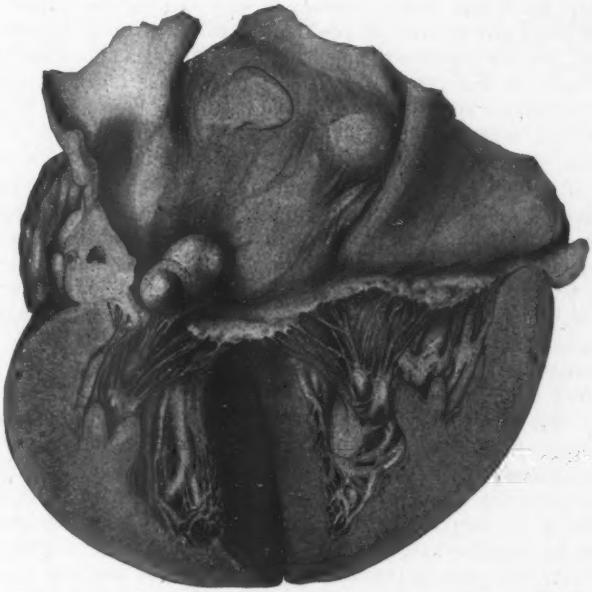

FIG. 1.—View of the interior of the heart showing the position of the tumor of the mitral leaflet.

FIG. 2.—Cut surface of the right half of the tumor of the mitral leaflet (actual size).

brown red. A definite capsule is seen to surround the tumor, except at its inferior hollow ventricular surface. The capsule starts from the insertion of cusp, and passes over the tumor to continue into one of the tendons.

A slice of the tumor was carried through alcohol, embedded in

celloidin, and sections were stained with hematoxylin-eosin, hematoxylin-van Gieson, elastin (Weigert), hematoxylin-muci-carmin, muchematin, and thionin.

Microscopically, the tumor is composed of loose connective tissue, in whose meshes there is a large amount of granular brown blood pigment, most of which is situated beneath the capsule. Scattered through the fibrous tissue are areas of star- and spindle-shaped cells. These areas give a faint but positive reaction with muci-carmin and thionin, but are negative to muchematin. They also take a deep blue stain with hematoxylin-eosin. The blood vessels of the tumor are large cavernous spaces originating and entering the tumor from its ventricular surface; they subdivide, and branches reach to the capsule. The walls of the bloodvessels are lined with a single layer of flat endothelium and contain a fine layer of elastic tissue. No elastic tissue is found in the tumor. The capsule of the tumor, which varies in thickness, is composed of connective tissue, with a fine network of elastic fibers. Its outer surface is covered with a single layer of flat endothelial cells. The inferior hollow ventricular surface, which is without a capsule, is covered by a single layer of flat endothelial cells.

Tumors of the valves of the heart have been described by Curtis,[1] Debove,[2] Ribbert,[3] Guth,[4] Leonhardt,[5] and Reitman.[6]

My case corresponds with these in that it contains mucin-reacting tissue, fibrous, and elastic tissue. Following these observers, one would call the tumor a fibromyxoma. But the lack of capsule on its ventricular surface, together with the aneurysmatic bulgings on the rest of the cusp, inclines one to view this not as a new-growth, but as an organized thrombus in an aneurysm of the mitral valve in which the capsule around the thrombus is nothing but the dilated cusp.

Examining the literature as given by Leonhardt, I find no report of a similar condition. As there is a difference of opinion as to whether all fibro-myxomas of the heart, and especially of the left auricle, are true newgrowths or organized thrombi on the basis of a former endocarditis, I report the case in the hope that this and observations on similar cases in the future may help to clear up the question.

[1] Arch. de physiol. norm. et path., 1871-72, iv.

[2] Myxome pédiculé développé sur la valvule tricuspidale, Bull. de la Soc. anat. de Paris, 1873.

[3] Neumann. Ref. i. d. Deut. med. Woch., 1904, Lit. Beil, S. 9. Ueber Rückbildung an Zellen und Geweben und über die Enstheung der Geschwülste, Biblioth. med. Abt. C., 1897, Heft 9; Geschwülstehere, 1904, S. 233, ff.

[4] Prager med. Woch., 1898, Nr. 8.

[5] Ueber Myxome des Herzens insbesondere der Herzklappen, Virchow's Archiv, 1905, clxxxi, 347.

[6] Ein Fall von primärem Klappentumor des Herzens, Zeitschr. f. Heilk., 1905, Heft 1.

THE POSTERIOR MEDIAN PLEURAL BOUNDARY, WITH REFERENCE TO GROCCO'S SIGN.

By W. J. Calvert, M.D.,
of Columbia, Missouri.

The normal relationship of the posterior median boundary of the pleural cavities to the vertebral column, œsophagus, aorta, and heart is of importance in a discussion of the physical causes of the paravertebral dulness, or the so-called Grocco's sign.[1] In anatomical and clinical literature little or nothing has been said on this subject. In consequence I have undertaken a study of the easily acces-

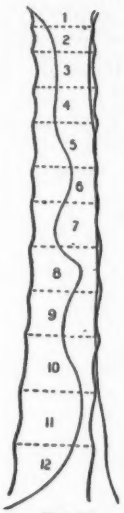

Fig. 1

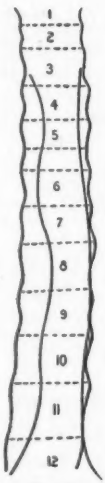

Fig. 2

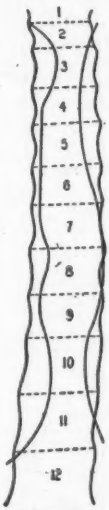

Fig. 3

Fig. 4

Fig. 5

sible anatomical material in our laboratory at Columbia and have charted the results. I wish here to thank Dr. C. M. Jackson for the use of his material.

The material considered includes 11 normal adults (Nos. 1 to 11); 1 newborn (No. 13); and 1 case of right-sided pleural effusion (No. 12). As the illustrations show clearly the course of both the right and the left pleural cavity, a description in detail is omitted.

The right pleural border in 11 of the 12 cases passes in front of the vertebral column varying distances often to the midline. In 1 case (No. 10) it extended entirely to the left of the column. The

[1] See Thayer and Fabyan, Amer. Jour. Med. Sci., 1907, cxxxiii, 14.

FIG. 6

FIG. 7

FIG. 8

FIG. 9

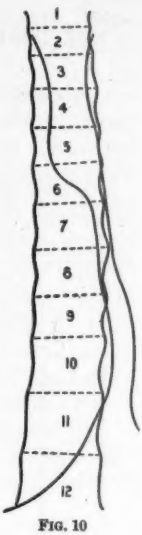

FIG. 10

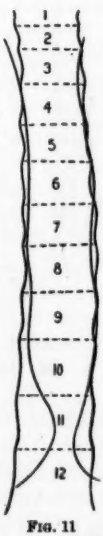

FIG. 11

FIG. 12

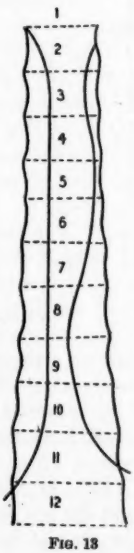

FIG. 13

Figs. 1 to 13 show a front projection of the dorsal portion of the vertebral column. The heavy lines represent the extreme limit of the right and the left pleural cavities.

Fig. 12 shows the border of the right pleural cavity in an old case of pleurisy with effusion. The degree of actual displacement to the left has not been determined.

Fig. 13 shows the pleural borders in a newborn. The relationship is the same as in adult life.

lower half of the line was further to the left than the upper. The left pleura did not extend on to the column to the same degree as the right most marked above and below, while the middle portion did not even touch the column. In practically every case the pleura was displaced toward the left by the descending aorta, especially from the fifth to the seventh vertebra.

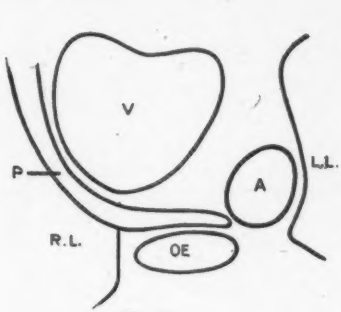

FIG. 14

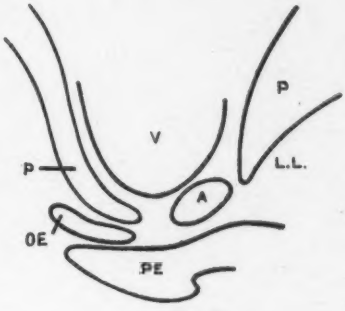

FIG. 15

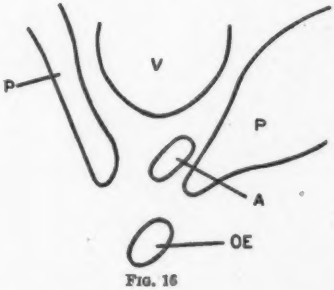

FIG. 16

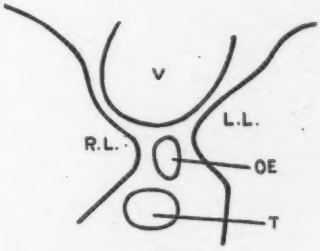

FIG. 17

The transverse sections show the relationship of the pleural cavities with the œsophagus, aorta, and heart, which is, of course, immediately in front of these structures. In Figs. 14, 15, 16, and 17 *P* represents the pleural cavity; *R.L.*, right lung; *L.L.*, left lung; *E*, œsophagus; *A*, aorta; *P.E.*, pericardium; *T*, trachea. Fig. 14 is a transverse section of Case 10 at the ninth vertebra. Fig. 15 is a transverse section of Case 2 at the disk of the seventh and eighth vertebræ. Figs. 16 and 17 are transverse sections of Case 13 at the ninth and fourth vertebræ, respectively.

THE DIAGNOSIS OF CEREBROSPINAL MENINGITIS BY CULTURES FROM THE BLOOD.

By J. M. Birnie, M.D.,

AND

M. T. Smith, M.D.,

RESIDENT PHYSICIANS TO THE GERMAN HOSPITAL, PHILADELPHIA.

At the present time the number of reported cases in which Diplococcus intracellularis meningitidis has been found in the general circulation is small—eight cases.[1] We report, therefore, the following case to illustrate the value of making a blood culture in all doubtful cases.

The patient, a female, aged fifteen years, entered the German Hospital May 5, 1907. The family history was negative. In the summer of 1906 the patient was in another hospital, where the diagnosis of acute articular rheumatism with acute endocarditis was made. She had a similar attack in the following December.

Five days before entrance to the German Hospital, the patient was suddenly seized with violent pains in the head, neck, arms, and legs, and she vomited repeatedly. These symptoms continued with more or less severity, except for the vomiting, up to the time of admission to the hospital.

On examination, she was a young girl of rather inferior development and poorly nourished. She was conscious of all that was going on about her. She seemed to be excessively tender all over her body, which fact rendered a satisfactory examination impossible. She would cry out whenever approached or touched. It was impossible to determine whether or not rigidity of the neck and Kernig's sign were present. The body was free from eruption. The area of the heart dulness extended from 2 cm. to the right of the sternum to the left midaxillary line. The apex beat was very diffuse, but was best seen in the sixth interspace. A whistling, systolic murmur was heard at the apex and was transmitted to the axilla. Except for the excessive tenderness and the heart condition, the physical examination was negative. The temperature was 102.4° to 103°; the white blood cells 34,800.

May 6, under aseptic precautions, a small incision was made over one of the superficial veins at the bend of the elbow and the vein exposed. The needle of an ordinary hypodermic syringe was introduced into the vein and 4 c.c. of blood was removed and distributed equally in two flasks containing 75 c.c. of sterile bouillon each. On May 7, the bouillon was found to contain a diplococcus which was isolated in pure culture on agar plates. The colonies were few and scattered and appeared round, flat, grayish,

[1] Simon, Jour. Amer. Med. Assoc., June 8, 1907.

translucent, moist, and shining. The organism decolorized by Gram's method. The presence of a Gram decolorizing diplococcus which grew on agar with the characteristics named above lead us to make a diagnosis of Diplococcus intracellularis meningitidis. On the strength of these findings a lumbar puncture was done and 50 c.c. of fluid withdrawn, in which intracellular diplococci, decolorizing by Gram's method of staining, were found.

On May 11, the patient's opsonic index to the diplococcus obtained from the blood, was 100 per cent., and she was given an injection of 0.5 c.c. of a "personal vaccine" standardized of 20,000,000 to the cubic centimeter. On that date her temperature was 103° to 103.4°. The following day the patient's temperature declined, and she was much brighter and ceased to cry out when approached. On May 15, her opsonic index was 172 per cent., and her temperature was 101.4° to 101.8°. Her temperature continued to fall by lysis and her general condition improved steadily. On May 17, her temperature reached 99.8° where it remained with slight variations until the 25th, when it reached normal and thereafter remained normal. The recovery was otherwise uneventful.

REVIEWS.

THE JOHNS HOPKINS HOSPITAL REPORTS. Volume XIII: Studies in Urological Surgery. By HUGH H. YOUNG, M.D.; H. A. FOWLER, M.D.; JOHN W. CHURCHMAN, M.D.; JOHN T. GERAGHTY, M.D.; LOUIS C. LEHR, M.D.; A. R. STEVENS, M.D.; STEPHEN H. WATTS, M.D., and F. H. BAETJER, M.D. Pp. 612. Volume XIV: Studies on Hypertrophy and Cancer of the Prostate. By HUGH H. YOUNG, M.D., Associate Professor of Genito-urinary Surgery, Johns Hopkins University. Pp. 629. Baltimore: Johns Hopkins Hospital Press, 1906.

THESE volumes, printed on a great deal of paper, consist mostly of reprints of articles which have appeared during the last few years in the *Johns Hopkins Hospital Bulletin*, and in a few other journals. Many of the articles have been elaborated, and a few, we believe, are now published for the first time. These facts are nowhere clearly stated in the present publications, and the reader who was not already familiar with current surgical literature could only infer that some of the treatises here included had heretofore seen the light of day from the fact that the cases reported and the references to literature somewhat mysteriously cease in 1904 or 1905, although the volumes did not appear until early in 1907.

Volume XIII covers a wide range of topics dealing with genito-urinary surgery, including twenty-one articles in all. Among the more valuable contributions are: II. The possibility of avoiding confusion by B. smegmatis in the diagnosis of urinary and genital tuberculosis, by Drs. Young and Churchman. VII. The treatment of stricture of the urethra, by Drs. Young and Geraghty. VIII. The treatment of impermeable stricture of the urethra. IX. The use of the cystoscope in the diagnosis of diseases of the prostate—both by Dr. Young. XI. Chronic prostatitis, by Drs. Young, Geraghty, and Stevens; and XII. A modern method for the performance of perineal lithotomy, by Dr. Young. Although many of the other articles contain matter of much merit, the limited space allotted to a review prevents reference to them.

In their studies as to the possibility of differentiating between B. smegmatis and B. tuberculosis, Drs. Young and Churchman show (1) the uncertainty of the staining and cultural methods at present employed; (2) that irrigation, performed according to a certain technique devised by them, is absolutely efficient in clearing

away all smegma bacilli, and (3) that all smegma-like bacilli which remain after this irrigation are truly the bacilli of tuberculosis. The technique employed is sufficiently simple, and they have had positive results in all the 104 examinations made according to this method.

Drs. Young and Geraghty, in their article on the treatment of stricture of the urethra, give some interesting and valuable statistics; but with all of their suggestions and conclusions few surgeons will agree. About 400 cases in all are analyzed. The results of gradual dilatation showed that of 17 patients who were traced after being treated more or less thoroughly, only 24 per cent. had recurrence; and 2 of these only after a period of eight years; whereas of 34 patients who returned for treatment during only a limited period, 67.7 per cent. had recurrence. Divulsion is condemned; internal urethrotomy is rarely employed, and then only for resilient strictures of the penile urethra. In 3 cases of impermeable stricture of the penile urethra, Dr. Young did perineal urethrotomy, and followed this by retrograde internal urethrotomy of the penile strictures. In 1 of these cases this method resulted in rupture of the urethra anterior to the strictures, necessitating external penile urethrotomy. The latter operation would probably have been quite satisfactory as a primary procedure; indeed we do not understand the delight the Johns Hopkins surgeons seem to take not only in doing a complicated operation when a simple would suffice, but also their passion for attacking strictures from the rear.

After perineal urethrotomy for strictures, they usually leave a catheter *à demeure* in the bladder, draining through the whole length of the urethra; in 2 cases only, was it allowed to emerge through the perineal wound; while in 9 patients no catheter was employed. In 1 case no instrument of any kind could be passed ten days after the operation, and another operation was done; it is not stated whether this unfortunate patient was one of those in whom the experiment was tried of leaving no catheter at all in the bladder. Among 79 operations there were 6 deaths; but as Dr. Young, with characteristic modesty, proceeds to explain, 4 of these were almost dead before operation, which reduces the mortality to 2.5 per cent.; while the remaining 2 deaths were really due to pre-operative conditions—the resultant of these forces being that about twelve pages later (p. 156) it is implied that *no patients* died after operation

Resection of the urethra was employed in only 2 patients, both traumatic cases: 1 patient, from whom 2 cm. of the bulbous urethra were excised with end-to-end anastomosis, was traced for seven years, and had then a urethra which admitted an 18 French sound —a remarkably excellent result. They urge, and we believe with propriety, that immediate perineal section be done in traumatic rupture of the urethra accompanied by much hemorrhage, even if there be no retention. We are not so sure that it will always prove wise to attempt "plastic repair of the injury" as a primary operation.

Certain statements in the article on impermeable stricture cannot pass unchallenged. That most surgeons are in the habit of abandoning perineal section (by which we mean external perineal urethrotomy without a guide) after a few aimless strokes of the scalpel, when they find it impossible, on exposing the anterior face of the stricture, to insert a guide into the urethral channel, and are then wont to attempt retrograde catheterism by means of suprapubic cyastotomy—is a statement which certainly does not describe the custom of most surgeons of experience in this city. Many facts tend to confirm us in our opinion that it will be immediately safer for the patient and more to his ultimate advantage, for the surgeon to stick to his perineal section and work it out on these lines if it takes all summer. But in saying this we do not wish it to be understood that we counsel the employment of so tedious an operation as perineal section, in patients who are acutely ill. For such cases—patients with impermeable stricture and acute retention—we have at our disposal a procedure to which Dr. Young witheringly refers as "dangerous, inaccurate, unsurgical, and particularly prone to lead to injury of the rectum." In thus describing the old operation of Dionis, so brilliantly employed and so widely popularized by Mr. Cock, of Guy's Hospital (Dr. Young spells it Cocke), it is very evident that the distinguished professor of genito-urinary surgery is not well informed either of the nature of the operation itself, or of the indications to meet which it was proposed. Dr. Young speaks of it as an "incision into the prostatic urethra blindly from the perineum and retrograde catheterization through the urethrotomy wound in that location." He says that after failure to find the urethra by perineal section, and because of the dangerous, inaccurate, and unsurgical nature of "Cocke's" operation, he has been driven, on several occasions, to perform suprapubic cystotomy and retrograde catheterism. Now everyone—except perhaps Dr. Young—knows that Cock's operation was not proposed as a sequel to, but as a substitute for, perineal section; and when so employed, especially in patients with retention (for whom indeed it is best reserved), there is no other operation which will relieve such patients so swiftly, so safely, and so pleasantly. We admit that perineal section is one of the most difficult operations in surgery, and that the surgeon often passes axious moments until, as the urine begins to flow, the bystanders see a look of relief pass over his countenance; but why Cock's operation should be so crushingly condemned because it is not suitable for what it was never intended, we cannot understand.

Dr. Young proposes, and has adopted in one case, a form of operation, which, while undoubtedly of value in patients without retention, can never, we think, take the place of Cock's operation in acute cases. This consists in exposing the membranous urethra to full sight, as in his operation of perineal prostatectomy, opening it, and dividing the impermeable strictures from behind forward. This

modification of the operation of John Hunter is certainly preferable to the suprapubic route, which Dr. Young considers the only alternative; and surgeons who are uable to dissect the urethra from before backward may be very glad to make the attempt to reverse the process.

One error in the volume, presumably a misprint, must surely be noted: the statement (p. 154) that Otis showed that the normal urethra frequently had a calibre of from 35 to 40 mm. Evidently what is intended is 35 to 40 French, or 35 to 40 *thirds* of a millimeter. Not even the enthusiasm of Otis could convince anyone that the normal urethra was ever over an inch and a half in diameter. Although this is one of the most glaring typographical errors, there are many others throughout the volume; indeed if the volume has received any editing at all, it is difficult to see in what it consisted.

Volume XIV contains only three articles: 1. Treatment of prostatic hypertrophy by conservative perineal prostatectomy. 2. Recto-urethral fistulæ. 3. The early diagnosis and radical cure of carcinoma of the prostate—all by Hugh H. Young, M.D. The text comprises less than 200 pages, the remainder—considerably over 400 pages—being composed of case histories, the records of 145 cases of perineal prostatectomy consuming no less than 334 pages. The object of this exhaustive analysis is, Dr. Young states, "to dissipate the false impression as regards the results in this country, and to remove the absolutely unjust, not to say false, idea of perineal prostatectomy which has been disseminated elsewhere." It will probably be news to many to learn that the results of prostatectomy in this country are regarded elsewhere as so deplorable; and the innuendo that a certain well-known British surgeon has been disseminating false ideas of the perineal operation, makes us earnestly hope that Dr. Young has not neglected to send him a copy of the present volume, bound in full morocco, with edges gilt.

Dr. Young's work is so well known, in this country at least, that extended mention of these articles is not necessary. The reviewer may be permitted to remark, however, that the great desideratum which a teacher should have in mind is not so much to impress his pupils with his individual skill and dexterity as to qualify them to go and do likewise. And those of us who sit humbly at the feet of the specialists, and watch with hungry eyes for the morsels which fall from their operating tables, note with regret the multiplicity of special instruments which Dr. Young now regards as indispensable to the proper performance of "his operation;" to wit: the cystoscope, the prostatic tractor, the new bifid retractor, a special posterior retractor, a special anterior retractor, and two special lateral retractors, not to mention the "enucleator" or special blunt dissector, the special lobe forceps, the special Halsted clamps to catch the urethral mucosa, and the Halsted operating table. We observe no mention of the best form of needle-holder for this operation, and presumably an ordinary scalpel is sufficient for most cases.

Among accidents which occurred during the operation, he mentions 4 cases in which false passages were produced by the *orderly* who held the staff in the urethra. Young complains of the trouble this made for the operator, but makes light of the disability caused the patient—in 2 of these cases only filiforms could be introduced after recovery from the operation; "but no definite strictures were produced" (p. 84).

Dr. Young's operative results are brilliant—he has now done 185 consecutive perineal prostatectomies, with only 7 deaths, a mortality of 3.7 per cent. It seems like painting the lily when he adds that in several of the fatal cases death was in no way caused by the operation; that in the last 100 cases there have been only 2 deaths, and that in the last 60 cases "there has not been a single death or bad result."

Perineal fistula persisted in 6 out of the 145 cases analyzed. The urinary functions were fully restored in all but 23 of the patients. It may be said, indeed, that only in about 14 per cent. of cases has the operation failed to give absolute relief, and that in all of these cases the postoperative condition is better than that which existed before the operation was done.

In closing it may be said that while Dr. Young is only presenting a study of his perineal prostatectomies, yet nowhere in all the volume does he even imply that there is the remotest excuse for the existence, still less for the adoption, of any operation other than that elaborated by himself. He refers to operations by any other technique as those done "blindly, blunderingly and barbarously, simply to save a little time." Yet what else than maudlin inconsistency, shall we call it, when he proposes, for the radical cure of recto-urethral fistulæ (7 cases of which have been encountered), an operation which has as one of its essential points suprapubic drainage of the bladder, which does away with "spasmodic efforts of urination"—thus tacitly admitting that suprapubic drainage procures rest for operative wounds in the region of the prostate.

Young's operation for radical removal of the prostate, neck of the bladder, seminal vesicles, and portions of the vasa deferentia has already been reported in the *Johns Hopkins Hospital Bulletin* (1905). He here records 4 cases of this operation, with "no operative mortality," although 1 patient "died six weeks after the operation as the result of an operative mistake." Even with a mortality of 25 per cent. (which Dr. Young is far from admitting), this operation should not hastily be condemned. Desperate diseases require desperate remedies; and if only the case reports convinced one that ultimate freedom from recurrence was assured, or that the patient's closing days were less distressing after the operation than if none had been performed, other surgeons would be more ready to adopt the extensive removal of the cancerous prostate advocated by Dr. Young.

A. P. C. A.

THE NURSLING: THE FEEDING AND HYGIENE OF PREMATURE AND FULL-TERM INFANTS. By PIERRE BUDIN, M.D., Professor of Obstetrics in the University of Paris. Authorized translation by WILLIAM J. MALONEY, M.B., Ch.B., Fellow of the Obstetrical Society of Edinburgh; with an Introduction by SIR ALEXANDER R. SIMPSON, M.D., LL.D., D.Sc., University of Edinburgh. With 111 diagrams in color and other illustrations. Pp. 199. London: The Caxton Publishing Co., 1907.

THIS remarkable series of lectures by Pierre Budin, now for the first time presented to English readers through Dr. Maloney's translation, constitutes one of the most valuable contributions to the study of the nursing infant that has ever been published. Budin is one of the few obstetricians who has seemed to realize that the newborn infant is something more than an annoying but relatively unimportant complication of the puerperal state. More than this, he seems to have taken a conscientious interest in the welfare and progress of the babies born under his supervision, and in this series of lectures to his classes has presented a most exhaustive study of the nursing infant that deserves the respectful attention of every physician whose practice brings him in contact with helpless babyhood. In no single publication do we know of such a wealth of material illustrating all possible phases of the natural feeding of the infant. Of especial value is the admirable presentation of the care and feeding of the weakling—the premature or congenitally feeble infant weighing at birth less than 2500 grams (5 pounds)—that should prove a revelation to many practitioners of more than average experience in obstetrical work. To the pediatrist this section cannot fail to be of extraordinary interest, emphasizing as it does the value of constant records of the infant's weight and temperature as a guide to its progress and an infallible warning signal of its danger.

The subject of wet-nursing is treated in masterly fashion, and its significant lessons should aid in saving many infant lives now ruthlessly sacrificed by careless obstetricians and incompetent nurses, to the latter of whom alone is too often entrusted the practical management of the important function of lactation, and whose one thought seems to be to get the baby upon a bottle as quickly as decency permits.

It is worthy of note, however, that Budin's experience has been gained among a class of patients with whom breast feeding is a normal and physiological result of maternity. Coming from the peasant and bourgeois classes, normality of infantile digestion is the rule, and it is safe to say that many of the difficult problems of infant feeding with which we of American experience are so familiar are practically unknown in Budin's clinic; furthermore, his patients, who are practically confined to those born in his wards, have not as a rule been subjected to dietetic experiments before

coming under his care. For these reasons we believe his experience in artificial feeding lacks many of the difficulties with which American pediatrists are so frequently confronted. His rule for all cases of partial or complete artificial feeding is to give sterilized whole milk containing from 3.75 to 4 per cent. of fat, in proportions to be determined by the weight and the rate of progress of the infant. Dilution of milk or any of the finer modifications is in his experience rarely required.

Commenting on the results of his observations under this plan of feeding, Budin asserts that he is "absolutely unacquainted with the so-called 'undiluted milk dyspepsia.' White stools of the consistency of putty, the pathognomonic sign of the new dyspepsia, indicate merely that the infant is being overfed. We never see them, for we do not overfeed. It is rarely that we need to prescribe more than 1000 to 1200 grams of milk, even for infants in their second year."

"As for rickets, not a single case has occurred in any of my consultations since I first began in 1892. Neither will you see eczema among our little patients. Since 1892 I have observed only 2 cases, both of which were suckled by mothers indulging in excess in food and drink.

"As for the so-called 'infantile scurvy,' which is alleged to follow the use of sterilized milk,.... I am still looking for my first case."

Such statements from a man of Budin's skill and experience are sure to attract a lively interest upon this side of the Atlantic; and while we believe that the conditions of infant feeding with which we are familiar are in many instances less favorable than those in which Budin has labored, his experience in what may be termed normal cases deserves the attention and close study of our most experienced pediatrists. One statement of his which is significant in this aspect of the subject is this: "As regards artificial feeding from birth, my experience is yet too limited to warrant any dogmatic statement of the most advisable method during the first few weeks of life. As I always endeavor to insist on breast feeding, my cases are not numerous enough to base any definite opinion upon. Probably in those infants who do not tolerate pure milk at the beginning, some form of digested milk, such as that which I used for weaklings, might be found of service." This is a confession which after all may serve to explain what at first sight seems a revolutionary dogma; and we are forced to the conclusion that digestive weaklings are a much more common class with us than they seem to be among the bourgeois of Paris.

With this commentary we most heartily commend this monograph to the American profession, believing that our methods of infant feeding have not by any means received a death thrust, but that both French and American students of the gentle art of race preservation may have much to learn from an impartial study of each other's successes. T. S. W.

THE PRINCIPLES AND PRACTICE OF DERMATOLOGY, DESIGNED FOR STUDENTS AND PRACTITIONERS. By WILLIAM ALLEN PUSEY, A.M., M.D., Professor of Dermatology in the University of Illinois; Dermatologist to St. Luke's and Cook County Hospitals, Chicago. Pp. 1020. With one colored plate and three hundred and sixty-seven text illustrations. New York and London: D. Appleton & Co., 1907.

IN taking up a new systematic work on cutaneous diseases one naturally is disposed to ask certain questions the answers to which will in a measure stamp the calibre of the work. Thus: What classification of the diseases does the author adopt? What innovations in general upon established custom are made? What is the nomenclature, new or that in common use? Is the author under the influence of foreign thought, or has he produced a work based largely upon experience in his own country? Such questions are generally solved without effort by perusing pages here and there, the author showing his hand plainly to him who reads between the lines. In the case before us the author has long been known as a laborious student and practitioner in the field of dermatology, and as one who not only is seeking the truth, but who aims to give expression to it in his writings. We should, therefore, expect to find much of interest in a systematic work like the present, and in this we are not disappointed. To give a synopsis of the contents would be impossible, but some of the more striking features may be referred to.

Much thought has been bestowed upon the subject of the principles of dermatology. A correct understanding and appreciation of these principles really mean everything to the clinician, and distinguish the casual observer of skin diseases (of which class there exist everywhere too many) from the skilled practitioner who comprehends the etiology and pathology of the disease before him as well as its treatment. We commend all that Dr. Pusey says on this broad subject, and anyone who reads this part of the book will be repaid for the time spent. In the classification we do not think the matter has been quite so happily dealt with, for some innovations upon long-established lines of thought have been made which at first seem to be inconsistent with the foundation stone of the structure. Thus, there is a class of "inflammations," one of "angioneurotic dermatoses," another of "dry, scaly, inflammatory diseases," and still another of "infectious diseases." This classification may be practical and in one sense it is so, but the method of thus grouping cutaneous diseases is a departure from the lines upon which we hold true classification should be based.

But, to proceed, the general view taken of the whole subject of cutaneous diseases is in the main in accord with that of most teachers in this country. Diseases, common and rare, are described much as occurs in the standard works of the day, and everywhere

may be observed an exposition, brief or lengthy, of the latest views upon etiology, pathology, and treatment. The subject-matter is thus brought well up to date. In the matter of treatment of some of the diseases we think more space might have been allotted to internal medication, diet, and the like. Thus, in the chapter on the internal treatment of eczema many more practically useful points (doubtless well known to the author) might with advantage have been elucidated. It is within the reviewer's experience to state that many excellent general practitioners not infrequently virtually ignore internal treatment in chronic eczema, with the result that the patients are neither cured nor benefited as they should be. The class of "dry, scaly, inflammatory diseases" includes lupus erythematosus, seborrhœic dermatitis, pityriasis rosea, psoriasis, lichen planus, dermatitis exfoliativa, and a few other less well-known diseases. As scaly eczema is not admitted to this class, and as lupus erythemotosus is usually regarded as being much more in its symptomatology than a scaly, inflammatory disease, this group does not seem to rest on a very solid foundation. In the class of "angioneurotic diseases" the most diverse cutaneous lesions occurring in different diseases occur, for here are found erythema multiform, herpes, pemphigus, pellagra, purpura, etc.

Considerable attention is bestowed on A. E. Wright's method of treating tuberculous and staphylococcic infections by the use of hypodermic injections of sterilized cultures of the bacteria, favorable results being reported in such diseases as furuncle, acne, and lupus vulgaris. In psoriasis, sodium cacodylate by the mouth in half-grain to one and a half-grain doses, thrice daily, has been found of value. The drug soon gives a garlicky odor to the breath, but does not readily disturb the stomach. The hypodermic method of administering arsenic is favored. Attention is directed to the not infrequent association of this disease with rheumatic and gouty states.

Among the new diseases described mention may be made of dermatitis vegetans, erythema elevatum, hydroa vacciniform, blastomycosis, and granuloma pyogenicum. Numerous other rare and foreign diseases are briefly described. It is gratifying to note the introduction of the eruptive fevers in the treatise. They assuredly belong here. The descriptions are brief, and, of course, with special reference to the skin. Many excellent photographs (mostly from Schamberg's collection) add greatly to the value of this chapter.

Scrofuloderma receives a special chapter, to which it is entitled, the author separating it from true tuberculosis. It might well have been longer, and made to include the small and the large pustular scrofulodermas. The former is described elsewhere, but the latter does not seem to be mentioned. The author prefers the French word "syphilide" to (it seems to us) the more correct and

in every way more desirable term "syphiloderm." It has always seemed that in connection with the English language the French word syphilide is out of place, and this for several good reasons. The author very wisely cautions as to the indiscriminate or careless use of the Röntgen rays. With his large experience in the employment of this therapeutic agent, caution deserves heed. The high-frequency current has proved disappointing to him.

The illustrations are unusually profuse, and, speaking generally, are satisfactory, most of them being originals, and many from the author's collection.

In concluding, it may be stated that a wide field is covered in the book, and that for this reason the author's task has been by no means an easy one. The subject matter is so abundant and varied that the physician, we believe, will derive more profit from its perusal than will the student. There is much more in the volume than the student can possibly digest. The author may be congratulated on the part he has played in advancing our knowledge of cutaneous diseases to a higher plane than heretofore. We bespeak a very kindly reception for the book. It deserves it. L. A. D.

A Laboratory Manual of Invertebrate Zoology. By Gilman A. Drew, Ph.D., Professor of Biology in the University of Maine; in charge of Zoological Instruction at the Marine Biological Laboratory, Woods Holl, Massachusetts. 201 pages. Philadelphia and London: W. B. Saunders Co., 1907.

Referring a laboratory manual of invertebrate zoology to a medical journal for review is suggestive of the growing interest of medical men in medical zoology and the relations of a large group of the lower animals to man in the matter of the production or transmission of disease. It is safe to predict that at no very distant date the work of instruction in our medical laboratories of bacteriology will be expanded to include a not inconsiderable amount of attention to the protozoa, as well probably to at least the medically important worms and arthropods and to various animals of higher types concerned in the transmission of human disease.

The volume in hand is intended as a laboratory handbook for beginners in invertebrate zoology and has no immediate application to medical problems, save as a medical man or student may care for a guide to laboratory study of these forms of animal life. It has been built up from a set of laboratory directions used in the instruction of the class in general zoology in the Marine Biological Laboratory at Woods Holl. Its especial value lies in the employment of the Huxleyan methods of study in the directions for observa-

tion, and in the questions for determination which are incorporated in the text under the various types set for study, thus not merely guiding in the systematic morphological study of types, but also stimulating an appreciation of the adaptations exhibited by these low forms. The classification followed is authoritative; the definitions modern and admirable; the instructions full and well adapted to student work, and the methods adopted simple and well selected. For use either by isolated workers or as a laboratory book in collegiate biological departments in the preparatory course leading to medicine, the book is to be strongly commended to favor.

A. J. S.

SURGERY OF GENITO-URINARY ORGANS. By J. W. S. GOULEY, M.D. Pp. 531. New York: Rebman Co., 1907.

THE author of this handbook discusses most of the subjects usually included in genito-urinary surgery. The volume is something more than a new edition of his monograph on *Diseases of the Urinary Organs*, published in 1873; chapters on orchitis, bulbo-urethral adenitis, and inflammation of the seminal vesicles have been added, and most of the other subject-matter has been brought up to date. The bulk of the volume consists of historical matter, and this is what lends it the only value it possesses. The other subjects have been treated more impartially and less theoretically in other recent publications.

A. P. C. A.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

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Green, Blue, Magenta, and Other Colored Urines.—Wm. Murrell (*Edin. Med. Jour.*, 1906, xix, 497) gives a rather extensive report of the various colored urines due to drugs or other causes, which may be of especial interest in relation to the modern synthetic therapeutic compounds.

Blue or Green Urines. A great majority of these are due to methylene blue. He found that ¼ grain twice a day imparts a pea-green color to the urine, and when repeated more often, the color becomes blue. These urines decompose slowly and the color which disappears may return on shaking, owing to the absorption of oxygen. All variations between the color of normal urine and that of deep blue may be seen. Green urines may at times be due to biliverdin and occasionally there are indigo-blue urines. The various tests and spectroscopic examinations are then given in detail for purposes of differentiation.

Black Urines. Carboluria: This may be due to carbolic acid or at times to salicylic acid in large doses. The urine is usually dark and smoky. Fuchsin in small doses may produce a dark olive-green urine, approaching black in color. *Melanuria:* This may be due to melaniasis, when there is present somewhere in the body a melanotic sarcoma. Other dark-colored urines may be due to hemoglobinuria and hematoporphyrinuria. The urine is usually of a dark port-wine color. Spectroscopic examination is here most important in distinguishing the cause.

Red and Purple Urines. Aside from the febrile urines which may give these colors to the urine there are certain drugs causing them, such as "Purgen" (familiarly known as phenolphthalein) and largely advertised as a purgative. When the urine is acid there is no color,

but when alkaline or neutral it shows a deep crimson-red color. This color is destroyed by acids and restored by alkali. The spectrum is quite characteristic. "Purgatin" is another synthetic drug that colors the urine a bright red in acid or alkaline urines. Pyoktanin, or methyl violet, usually gives a faint violet tinge to the urine. Fuchsin produces a bright-purple urine. It may be readily distinguished from phenolphthalein by the disappearance of its color on the addition of alkalies and the appearance of a yellow color with acids. Murrell gives the various tests for the different drugs and shows in plates their spectra as compared with the solar and urinary spectra.

[Under black urines the author might have mentioned alkaptonuria in which, on standing, the urine may become nearly black.—W. S. T.]

Experiments on the Leukolytic Action of the Blood Serum in Cases of Leukemia Treated with the X-rays and the Injection of Human Leukolytic Serum in a Case of Leukemia.—J. A. CAPPS and J. F. SMITH (*Jour. Exp. Med.*, 1907, ix, 51). The general conclusions which Capps and Smith give in this excellent piece of experimental work are as follows: "The *x*-rays produce in leukemia a disintegration of the leukocytes, affecting especially the young forms, namely, the myelocytes and the non-granular mononuclear cells. A similar action but one of less degree takes place in leukemic blood exposed to the *x*-rays in vitro. The serum of a leukemic patient who has improved under the *x*-ray treatment when injected into animals causes leukopenia; when added in a hanging drop to the leukocytes of another individual, it disintegrates the cells. This leukolytic action is selective, destroying first the mononuclear cells. The strength of the leukolytic action seems to be proportional to the degree of clinical improvement of the patient under the *x*-ray treatment. The serum in a case of leukemia which has been exposed to the *x*-rays has a marked agglutinating action on normal red corpuscles and on other corpuscles. The degree of agglutination varies roughly with the degree of leukolysis. The *x*-ray treatment of normal or leukemic blood in vitro does not materially alter the phagocytic power of the leukocytes. The injection of a strong leukolytic serum from a patient suffering from lymphatic leukemia under the *x*-ray treatment, into another individual with lymphatic leukemia but not under treatment, causes a decided and rapid fall in the number of the leukocytes, the mononuclears being principally affected. With repeated injections, a partial immunity to the serum was established." The nature of the leukolysin remains in doubt. It may be an amboceptor-complement complex or a true toxin.

Review of 105 Reported Cases of Acute Pancreatitis with Special Reference to Etiology; with a Report of 2 Cases.—A. EGDAHL (*Johns Hopkins Hosp. Bull.*, 1907, xviii, 130) gives a most careful review of the reported cases of acute pancreatitis with special reference to the etiology, and in summing up notes that the onset was sudden in most of the cases, due to whatever causes, and corresponds closely to the original description of Fitz. As regards the mortality: Of the 44 cases associated with gallstones, 30 died. Of the 32 associated with gastro-intestinal disturbance, 17 were fatal. Of the remaining cases due to miscellaneous causes, 29 in all, 12 died. Sugar was present in the urine of 6 cases;

3 recovered; 2 died. In 1 there was no statement as to the results. Fat necrosis was present in nearly all of the cases operated on or seen at autopsy. As reviewed from the articles in the literature Egdahl notes that the pain is most probably due to the stretching of the sensitive parietal peritoneum, especially where there is much extravasation of blood, and this spreading may account for the different localizations of the pain. The inflammatory process does not necessarily follow the same route as the hemorrhage. The cause of the marked collapse in death has recently been shown to be most probably due to the absorbed trypsin. Egdahl reports on 2 cases of which he has the notes, 1 of acute hemorrhagic pancreatitis in which there was marked inflammation about the pyloric end of the stomach and duodenum, with some occlusion of the ampulla of Vater. No gallstones were present at autopsy, but may have been previously. Fat necrosis were present. The second case was one of acute suppurative pancreatitis in which typhoid fever was most probably the cause. In this latter case sugar was present in the urine and fat in the stools. The head and body of the pancreas were much destroyed. There were no gallstones present.

His conclusions are as follows: (1) Gallstones are probably the most common single cause of pancreatitis. Judging from this series about 42 per cent. of the cases of acute pancreatitis are associated with gallstones. (2) Gastro-intestinal disorders are the next most common cause of acute pancreatitis. In this series of cases about 30 per cent. belong to this group; 17 out of the 32 of this group gave a history of alcoholism. It is very propable that retrojection of bile may be caused by intestinal disorders closing the papilla of Vater. (3) Acute pancreatitis may be caused by many other conditions. Among these we have typhoid fever, tuberculosis, mumps, trauma, syphillis, emboli, appendicitis, malaria, and gastric ulcer. (4) The organism most commonly present is B. coli communis; next comes the streptococcus and the staphylococci. (5) Typhoid fever is the most common of the acute febrile diseases present according to the previous histories of these cases of atute pancreatitis. In the present series 3 were directly associated with typhoid fever alone and 4 had suffered from typhoid fever some time before the onset of acute pancreatitis and had apparently recovered; another had had typhoid fever and erysipelas. But 2 out of these 8 cases were associated with gallstones. It should be kept in mind that in this latitude typhoid fever is the most common continued febrile disease.

The Treatment of Tuberculosis by Marine Climates.—Wm. Ewart (*Medical Press and Circular*, London, 1907, lxxxiii and lxxxiv, 447 and 476) begins this thorough analysis of the effects of marine climates by the following summary of cases suitable for such treatment: (1) All cases of surgical tuberculosis and scrofula are suitable. (2) All latent or threatened cases are suitable.. (3) Early cases of declared tuberculosis are debatable. They are all fit to try the mountain cure, but failing in this not all will benefit most at the sea-side; and more equable climates may be indicated. (4) The suitability of cases of advanced phthisis can only be decided in relation to the existing prognosis and to personal toleration and preference in regard to climate. (5) The excellent progress maintained at chosen spots along the coast by some cases of chronic

quiescent phthisis reveals the fact that there are temperaments for which sea-side air is especially favorable, and may be of positive advantage even at the later stages. Ewart goes carefully into the different aspects and effects of sea-air and sea-water, also the different qualities of pure ocean air and sea-coast climates in tuberculosis, and in summing up, his conclusions are that in most cases the inland and altitude cures are more beneficial, but in certain other cases the marine climate is the best, and this latter is of the greatest benefit in the prevention of the disease in suitable subjects. He says that in England especially the best place for the "prevention sanitarium" or "preventorium" is the sea-coast.

Tertiary Syphilitic Fever and the Visceral and other Changes Connected with It.—PARKES WEBER (*Lancet*, 1907, i, 728) reports extensively several cases bearing on the above points, in the first one of which a female on four different occasions showed a remarkably rapid disappearance of the fever on the use of antisyphilitic treatment. The fever is usually of a hectic type and in many cases may often be mistaken for some septic condition or even pulmonary tuberculosis, especially as the fever is sometimes accompanied by chills, night-sweats, and emaciation. Many examples of such cases are reported from the literature. As noted in the accompanying article the diagnosis of typhoid is sometimes made and especially when associated with diarrhœa. Endocarditis may at times be suspected. The associated liver conditions, with pain, tenderness, and even jaundice, may lead at times to a suspected abscess, cholecystitis, etc., and operation may often be tried. Gastrointestinal symptoms in late tertiary syphilis may be very severe and associated with fever, cachexia, anorexia, and obstinate diarrhœa. Obscure bone and joint conditions may often be due to a luetic infection, and when associated with some pyrexia may often be misleading, but clearing up on active antiluetic treatment. Weber gives numerous reports from the literature, with cases and types of fever associated with various obscure visceral manifestations of lues.

This article leads up to the review of another similar article entitled "Two Cases of Syphilis Simulating Typhoid Fever," by D. ROLLESTON (*Med. Press and Circ.*, London, 1907, lxxxiii, 307), who says that the possibility of syphilis being mistaken for typhoid fever has been recognized since Fournier in 1873 emphasized the similarity of the two conditions and introduced the term "typhose" to designate the condition in certain cases of syphilis, particularly in women, which closely simulate typhoid fever. He also gives a brief *resume* of the literature on this subject and notes that, though rare, some of the cases resemble typhoid, especially those with enlarged spleen, abdominal distention, and others with diarrhœa. An interesting reference is to those cases reported by FUTCHER (*New York Med. Jour.*, 1901, p. 1065). The fever may exist apart from any specific manifestations, and to this manifestation Fournier gives the name "essential syphilitic fever." The disease may be mistaken for tuberculosis, malaria, or influenza. Typhoid fever and syphilis may co-exist and a persistent negative Widal reaction may help in excluding typhoid fever; mercury and iodide may be of service. The cases reported by Rolleston were admitted to the hospital with a diagnosis of typhoid fever, the first with

a low grade of fever and with marked cerebral symptoms resulting fatally. Rolleston calls attention to the following points in connection with the first case: (1) The tendency that syphilis has to imitate other diseases, as in this case before admission, the diagnosis being, first, diphtheria; second, brain disease; and lastly, typhoid, for which he was admitted. (2) The early implication of the brain. (3) The galloping character of the disease. (4) The intermittent type of fever. (5) The enlargement of the liver. In the second case the general phenomena and the steady high temperature suggested typhoid fever at first, but in a short time typical luetic manifestations appeared. This patient recovered quite rapidly on active antileutic treatment.

The Diagnostic and Prognostic Value of the Enumeration of the Nuclei of Neutrophilic Leukocytes and their Relative Phagocytic Power.—D. M. KAPLIN (*New York Med. Jour.*, 1907, lxxxv, 674). As is well known the nuclear polymorphism of the neutrophilic cells extends all the way from a mononuclear form to a form having two or more parts. Arneth in particular took up the study of the relationship of the number of the nuclei of different cells in various diseases. The simple indented and bent mononuclear is most probably the closest to the myelocyte and the youngest of the polymorphonuclear cells. As noted by Arneth the cells predominating in number are those containing two or three nuclei; next, those with one nucleus; then those with four nuclei, and lastly those with five nuclei. In certain pathological states the number of twos and threes may be diminished and those with one nucleus markedly increased. The normal arrangement of figures as regards the number of nuclei may be graphically shown in a count of 100 cells as follows:

Number of nuclei,	1	2	3	4	5
Number of cells,	24	45	25	5	1

Kaplin has been led by this division to make careful nuclear counts and to determine the relation to prognosis and diagnosis in various diseases. He has noted that in the beginning of a disease there is a rapid rise in the count of the one-nuclear cells which increases as the disease gets worse and remains stationary when the disease is stationary. With the subsidence of the disease the number of mononuclear cells diminishes gradually and the binuclear or polynuclear cells increase. He cites many cases with their nuclear counts which bear out these statements and says: "No matter what the number of white blood corpuscles per cubic millimeter, the nuclei of the neutrophiles apparently behave in a constant and regular manner in infectious processes or in any condition where the organism is below par, so that we have a delicate hemic gauge whereby to distinguish an infectious process in low-par states, when a hyperleukocytosis may be absent." The nuclear counts vary apparently with a reinfection or a relapse during the disease. As far as assigning any function to this mononuclear form, he can only offer hypotheses, such as that the extra-formation of these young forms meets the added demand in infections, or that the disease paralyzes the further development of these cells.

As regards the ability of the different nucleated cells to take up bacteria

the author performed some experiments with staphylococci and found definitely that the mononuclear form takes up more bacteria than the others, the next in order being the binuclears and trinuclears, those taking up the least number being those with four or five nuclei. This may be graphically shown as follows:

Number of nuclei,	1	2	3	4	5
Number of cells,	32	30	28	10	0
Number of staphylococci in cells,	160	135	126	18	0
Average to a cell,	10	9	9	3.6	0

Kaplin notes in conclusion that this is only a preliminary communication, and says that much further work is needed on this interesting subject.

The Occurrence of Atypical Phagocytic Cells in the Circulating Blood.—M. W. ROWLEY (*New York Med. Jour.*, 1907, lxxxv, 674). The recent review of an article by van Nuys, in the *Boston Medical and Surgical Journal*, on the presence of atypical phagocytic cells in the blood, brings up this article for review as indicating the possibility of a more frequent occurrence of these atypical cells if only looked for and noted carefully; and by more careful and extensive reports of many such cases much light may be thrown on clinical hematology. Rowley in one case of tertian malaria and three cases of lymphatic leukemia found these atypical phagocytic cells. They varied much in size and shape, sometimes being round and sometimes irregular in outline and shape, with protroplasmic processes. They may have one or more nuclei, the nuclei containing a fine reticular network, and in the majority of the cells being kidney-shaped. In staining by Wright's method the cells resemble the large lymphocytes, the nuclei staining a reddish purple and the protoplasm various shades of dusky blue. There are usually no distinct granulations. The cells may be seen with red blood corpuscles and even other leukocytes engulfed. As to their nature, they resemble to some extent the elements found in exudates into the serous cavities or in the spleen and elsewhere; that is the so-called "endothelial cells." The article has several photomicrographs of these atypical cells, and their presence and phagocytic properties have been identified by good authorities.

[In pernicious estivo-autumnal malaria the presence in the peripheral blood of enormous macrophages is the rule.—W. S. T.]

Cervical Adenitis with Reference to Mouth Infection.—F. D. DONOGHUE (*Boston Med. and Surg. Jour.*, 1907, clvi, 392) asserts that the frequency with which purulent conditions of the teeth and mouth are overlooked is most important, as in a great many diseases the beginning of the trouble dates from a mouth infection or pyorrhœa alveolorum, which leads first to the involvement of the cervical glands. In reviewing the literature as to the origin of pulmonary tuberculosis he notes that primary tuberculosis of the cervical glands is quite rare, and in a study of 300 cases of enlarged cervical glands at the Boston Dispensary says that in very few cases only should the source of the infection be overlooked, and

in all cases before the glands actually disintegrated treatment of the primary cause in the mouth affected a cure. Donoghue then gives a careful description of the various groups of glands of the neck, the parts they drain, and the disease processes they may easily absorb. His conclusions, based on 300 cases, are as follows:

"Enlarged glands of the neck are not primarily tuberculous, and bear the slightest relation if any, to the general or pulmonary tuberculosis. They are due to a mixed infection of pus-producing bacilli. They will quickly resolve if the source of the infection is removed before the glandular tissue becomes disorganized. The treatment in the later stages, especially, is entirely local and surgical, either opening and draining, or, in advanced cases, complete dissection. General hygienic measures should, of course, accompany it."

SURGERY.

UNDER THE CHARGE OF

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Traumatic Curved Radius, with Progressive Subluxation of the Ulna.—DERSCHEID-DELCOURT (*Jour. de chir, et annales de la Soc. Belgæ de chir.*, 1907, vii, 235) reports a fracture of the radius consequent upon the violent backward turn of the crank of an automobile. In attempting to start a recalcitrant machine he received all at once a shock which he could not control. Severe symptoms followed and the skiagram showed a fracture of the lower third of the radius. There was a wedge-shaped fragment from the ulnar side of the radius, the apex being toward the radial side and the base toward the ulnar side of the forearm. The handle of the crank being held in the fork between the thumb and the fingers, the shock was transmitted through the radial portion of the carpus to the radius, which was thus caught between the carpus and the humerus. To this action was added, probably, that of traction on the lower end of the radius by the anterior carpal ligament. The kind and degree of force in this accident are peculiar to the automobile. The treatment consisted chiefly in retaining the limb in a plaster bandage longer than the usual time, because of the slowness of consolidation. In about eight weeks massage was begun. The skiagram had shown a slight angulation at the seat of fracture, the lower fragment being pushed outward while the upper was directed toward the interosseous space. There was now observed a progressive subluxation of the carpus from the ulna. As the consolidation of the radius progressed, the skiagram showed that the radius became more

and more curved inward and forward, and the ulna more separated from the wrist. The ulna was carried backward, the ulnar portion of the wrist being carried strongly forward. The writer explains the mechanism of the deformation by the presence of the triangular or wedge-shaped fragment on the ulnar side of the radius and the gradual tendency of the chief fragments to approximate each other for the production of callus. This progressive shortening and angulation of the radius led to the disarticulation and deformity of the wrist. There is partial functional impotence, that is, supination is very limited, but all the other movements are perfectly free. The patient is, however, considerably distressed by this loss of function, particularly his inability to use the gun in hunting, of which he is very fond, and by the pain on pressure and deformity. Massage and passive movements have been tried. A brace is being employed to support the whole forearm and wrist, furnished with a strong steel spring to keep the wrist reduced. A metallic plate with a pad over the prominence and elastic bands are used with the hope of finally correcting the curve in the radius. Considerable progress has been made already, although the limb is far from being normal. As a last resort, if the cure remains incomplete the writer thinks it will be advisable to do an oblique osteotomy of the radius, advised by Duplay and given in detail in the recent work of Gyselynck and Lemoine upon the reparative surgery of the hand.

Neuralgia of the Sciatic Nerve Due to the Pressure of a Dermatoleiomyoma.—De Beule (*Jour. de chir. et annales de la Soc. Belg. de chir.*, vii, 1907, 239) reports a case in which a woman, thirty-seven years old, suffered for years from a sciatica intense and rebellious to all medical treatment. The neuralgia involved the region supplied by the external popliteal sciatic (peroneal). There were no atrophic troubles; muscular power, circulation and sensation were completely normal, and none of Vallieux's points were detected. On the external surface of the knee above the head of the fibula was discovered a small hypodermic tumor, the size of a cherry. It was without pain to superficial pressure, but on strong pressure there was an attack of the typical neuralgia, although the patient had never suspected that the tumor had anything to do with it. It was excised without injury to the nerve and found to be grooved on its under surface for the passage of the nerve. Except for a slight flattening the nerve was otherwise normal in appearance. Without special reason for doing so De Beule stretched the nerve. The cure was immediate and complete. Histological examination showed the tumor to be a fibroleiomyoma. In several cases it has been shown that these myomas are remarkably sensitive to pressure or become the seats of very troublesome neuralgias, occurring spontaneously from cold or from external irritation. The explanation of this is probably to be found in the contraction of the muscle upon the nerve filaments. The etiology and pathology of these tumors is not known.

The Use of Animal Blood Serum in Surgery.—Stuart-Low (*Lancet*, 1907, i, 1221) has been using the old oiled-silk dressing applied directly to recalcitrant wounds. The good results in a number of such cases

impressed him very much. In trying to explain the results he came to the conclusion that they must be due to the blood serum (or lymph) and the assistance given to the surface circulation. A dry dressing in contact with a healing wound absorbs the normally exuding serum and becomes adherent to the growing tissues. It thus blocks the exudation and therefore the surface circulation and dries the granulations. The oiled silk does not, and keeps the wound always bathed in serum, thus aiding the superficial circulation in the healing region. This dressing, once in common use in surgery, went out of practice because it cannot stand boiling or immersion in strong antiseptic solutions. The writer simply washes in sterilized or boric solution before applying it to a wound. Being impressed with the theory of opsonins and the practical application of them, he argued that if so much depends on the blood serum, it would be well to increase the amount of it in and about wounds; to employ it as the fluid to sluice, irrigate, and dress wounds. To test this view he obtained a quantity of fresh blood from the butcher, the blood being poured directly from the aorta of sheep into sterilized vessels. This was kept in air-tight glass jars. It was mostly in ear cases that he used the serum. It is particularly suited to these, since there is so much bone excavation that a dry instead of a weeping wound results. Desiccation is usually inimical to the ready healing of a wound, and this is successfully avoided when the serum is employed. In every instance the soft structure healed by first intention.

Clinical Remarks on the Operative Treatment of Fractures.—LANE (*Brit. Med. Jour.*, May 4, 1907) says that while recent fractures of the femur can usually be readily and effectually dealt with by operation practically without risk, the surgical treatment of malunited fractures of this bone is often difficult in the extreme. It occasionally causes some anxiety because of the profuse hemorrhage which may take place during the operation. In oblique ununited fractures Lane generally makes an oblique section of the fragments, rather than to freshen the fractured surfaces with the curette or chisel, or to make a transverse saw-cut which would in most cases sacrifice too much length of the bone. Much care is usually requisite in determining the plane in which each fragment must be divided. The fragments are then splinted together with plate and screws.

Fracture of the epiphyseal line of the head, or separation of the upper epiphysis of the femur, is rarely recognized at the time of the injury. Secure union is effected by an abundant callus with great rapidity. The patient suffers from two disabilities: an excessive outward rotation of the lower limb and an impaired function of the hip-joint. Lane has many times operated on these fractures. The capsule is exposed and the anterior ligament cleared and defined. If the stump of the neck is excessively prominent, as it usually is, enough is taken from it to allow more complete range of flexion. The outward rotation of the shaft is overcome by lacing up the anterior ligament transversely to the length of its fibers by silver wire. This approximates the points of attachment of the ligament until the range of rotation of the limb equals that of its fellow. The results have been to bring the limb nearly to the normal in function and appearance.

Concerning Suture of the Patella and its Technique.—Hausch (*Zent. f. Chir.*, xxxiv, 1907, 530) says that an increasing number of surgeons are suturing the fragments of a fractured patella soon after the accident. The general rule is to operate if the extension apparatus is seriously damaged, but not if the patella alone is broken. The usual test of the power of extension is the ability or the lack of it to lift the extended limb from the bed. The degree of separation of the fragments has some value. Hausch, however, shows by one case, operated on thirty-six hours after the accident, that complete loss of function may exist with only a slight tear, 1 cm. from the patella, of the lateral ligament of one side. He thought that if operation had been delayed a few days the patient would have been able actively to extend the limb, and that the loss of function in this case was due to the freshness of the fracture, that is, to the pain which prevents contraction of the quadriceps, as well as flexion of the joint. Operation was, however, indicated in this case because the lower fragment was split into several smaller fragments the union of which would probably have been disturbed by the massage and passive movements which would have been practised even if operation had not been done. Hausch agrees with Thiem that primary suture of a fractured patella is indicated not only when the lateral expansions of the quadriceps are torn but whenever a gap can be detected between the fragments, The transverse incision is exposed to the danger of infection of the fracture and the joint through a suture and to pressure on the scar in kneeling. The only objection to the large cured incision above the patella is that the flap may become detached later, but if careful hemostasis is observed, this will not occur. If it is made to consist of fascia and skin it will have a sufficient blood supply. He uses thick silver or albuminium-bronze wire, and at least one of the sutures is passed through the whole thickness of the bone into the joint. If one fragment is too narrow or splintered, the suture should surround the borders of the fragment as was done in the case described in this paper. When there is no splintering of the fragment, the other three sutures are passed obliquely through the bone so that they do not involve the joint. He always sutures over the fracture the periosteum and overlying fascia, and the lateral expansion with silkworm gut. Most surgeons dress the limb in extension and begin passive motion in about eight days, some wait three weeks (Franz Koenig) and even four weeks. Moullin, however, does not immboilize the knee after the suture, beginning as soon as possible with massage and passive motion, and permitting the patient to stand in three weeks. In recent times Hausch has begun massage of the quadriceps seventy-two hours after the operation with careful passive motion; although he has had some anxiety concerning refracture or tearing of the sutures. He has never observed it, however. Von Bruns has shown by skigrams that the sutures frequently tear out, and Hausch thinks this is due to strong tension put upon the sutures by attempts at flexion. In the cases which he has seen many weeks were required to obtain right-angled flexion. For this reason he places the knee at an angle of about 100 or 110 degrees as soon as the sutures have been placed in the fragments and lateral ligments. If they do not tolerate this degree of tension they are then loosened and retightened with the knee in

that position, which the sutures will tolerate. The wound is then closed, a compress applied, and a suitable dressing to keep the limb in flexion. On the day of the operation massage is applied to the thigh and leg, and in forty-eight hours gentle passive motion. Extension can be made complete with ease, while flexion can be carried from the primary position about 10 to 20 degrees. Gradually the patient is permitted to employ active movement in the knee. Eight days after the operation the sutures are removed and on the fourteenth day with a supporting bandage he is permitted to stand up. Hausch believes that this not only hastens functional healing, but is a safer method.

An Advantage of Operation in the Acute Stage of Appendicitis.—LILLIENTHAL (*Amer. Jour. of Surg.*, 1907, xxi) considers that operation in the usual "acute appendicitis" is practically as safe as in the interval. In the interval we practically make a well man sick, while the individual suffering from the acute disease has his forces, opsonins, and leukocytes prepared for a more serious battle than that with the surgeon. To such a patient the operation comes as a comparatively little thing, and if no error in technique mars the surgeon's work, relief is immediate and convalescence speedy. The operative statistics, always excepting cases of perforation, thrombosis, gangrene, etc., are quite as good as in the interval operation; and if perforation, thrombosis, or gangrene is present, it simply means that operation was all the more indicated.

Report of a Dislocation of the Upper End of the Fibula.—GOLLEY (*Amer. Jour. of Surg.*, xxi, 1907, 171) says that there have been about 25 recorded cases of dislocation of the upper end of the fibula. He reports a case in which a man, weighing one hundred and eighty pounds, slipped and, after sliding, sprawling, and twisting, finally landed in a sitting position with his left leg under him. At the same time he felt something snap. On the following day by flexing and extending the foot a grating sensation was felt in the calf of the leg. By palpation an outward and forward dislocation of the upper end of the fibula was discovered, which became displaced as much as or more than the width of the bone whenever the foot was flexed or extended. A plaster cast was applied and left in place for three weeks, when the dislocation was found cured.

The Pathology and Treatment of Appendicitis.—ALBU (*Mitteilungen a. d. Grenzgeb. d. Med. u. Chir.*, 1907, xvii, 349) says that all cases of appendicitis, in which signs of peritoneal irritation are present, severe or suspicious, should be operated on as soon as possible. The time of operation will be decided by the occurrence of the first perceptible warning symptom of the threatening peritonitis. There is a large number of acute cases of appendicitis, which in a few days will subside spontaneously and be cured, in many cases permanently. There is nothing to justify a fundamental rule for early operation in all cases of acute inflammation of the appendix. In mild cases the dangers of the disease are not greater than those of operation. Early operation in the first twenty-four or forty-eight hours must naturally lead to many errors in diagnosis, since the symptoms at this time, especially in mild cases, are not well developed.

The statistics of early operation have no decisive value, since they include many errors in diagnosis and also the mildest cases. The presence of an appendicitis can be accepted only when the appendix shows macroscopical changes. In the treatment of perityphlitis, even of the mild cases, the use of opium and purgatives are to be avoided. In chronic intermittent and remittent perityphlitis the operation is always indicated, and the earlier the more severe the attack or the symptoms complained of. In lingering chronic appendicitis the operation is to be advised if the objective symptoms (constant resistance and tenderness on pressure at the typical place) are present. When, however, the subjective symptoms only are present, a longer trial should be given to internal therapy, which in such mild cases often leads to permanent healing.

Investigations Concerning the Etiology of Appendicitis.—KRETZ (*Mitteilungen a. d. Grenzgeb. d. Med. u. Chir.*, 1907, xvii, 1) says that in November, 1900, he had the opportunity of doing postmortems on three cases of appendicitis one after the other. One of them died one year after the attack, from traumatic tetanus. The others were severe acute fatal cases, terminating in a phlegmonous condition of the appendix and septic peritonitis. Adrian believes that there is an intimate causal relation between tonsillitis and appendicitis. Kretz supports this view on the basis of his observations. Adrian considers the tonsil as the primary focus which gives rise to a bacteremia and that to an appendicitis. Of 3579 postmortems at the Kaiser Franz-Joseph Hospital, 53 were in cases of appendicitis. Of the 53, 19 showed signs of recent acute phlegmonous inflammation. Of these 19, in 14 a complete anatomical examination was made, while in 5, for certain reasons, the neck was left alone. The 14 which were completely examined showed, besides the fatal appendicitis with septic peritonitis, a tonsillar angina. Bacteriological examinations showed, in 12 cases, streptococci in the tonsil and intestine and peritoneum. The changes in the tonsil in these cases are marked, uniform, and typically inflammatory. Kretz's investigations lead to the conclusion that phlegmonous appendicitis can be considered anatomically as a disease resulting from tonsillar angina. He feels convinced that the dominating importance of the pyogenic infections associated with anginas is very imperfectly appreciated. In 1903 he saw 11 such cases without wounds, 15 puerperal processes, and 25 erysipelas cases; not less than 14 acute and 23 subacute pyogenic infections, which took origin from the lymphatics of the throat. The acute fatal cases were 3 phlegmonous anginas, 2 tonsillar pyemias, 1 purulent basillar meningitis, 4 phlegmonous appendicitis cases, 2 of osteomyelitis, and 2 of ulcerative endocarditis. The 23 subacute consisted of 8 cases of endocarditis, 4 pleural empyemas, 2 of osteomyelitis, and a suppuration of the gall-bladder from gallstones. These important and frequent diseases, on account of their various anatomical forms, are not considered by most physicians as being related to each other. They are related to each other, not only as they may be due to one pyogenic microörganism etiologically, but they may belong to the same epidemic group in which the point of contagion is in the angina.

THERAPEUTICS.

UNDER THE CHARGE OF

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Bier's Hyperemia in Acute Gout.—ALKAN (*Die Therapie der Gegenwart*, 1907, i, 43), on the ground that blood serum is one of the best uric acid solvents, has applied artificial venous stasis according to Bier's method in the treatment of attacks of gout. This treatment, in connection with local applications, is followed by rapid cessation of the seizure. It is advised to associate alternate local applications of heat and cold with the treatment by stasis. The constriction of the part is kept up for two or three hours, the limb being elevated, and cold compresses are applied, to be followed by hot applications for an equal length of time.

Antisyphilitic Treatment in Diabetes Insipidus.—VAPHIADES (*Revue de méd.*, 1907, iii, 296) reports a patient twenty-nine years old, syphilitic for five years, who suddenly became affected with excessive thirst and polyuria; four months later the patient had become markedly cachectic and the urinary conditions persisted in spite of ordinary treatment. At this time the hypodermic administration of mercury protiodide, $\frac{3}{4}$ grain daily, was begun, in connection with the internal administration of potassium iodide in doses of 30 grains daily. After two months of treatment the patient was completely cured.

Gelatin in Melena Neonatorum.—HEYN and SCHUBERT (*La semaine méd.*, 1907, viii, 94) have employed gelatin in intestinal hemorrhages in infants; it is administered subcutaneously, and one patient, an infant of four days, who exhibited icterus and hematemesis, recovered rapidly after two injections, on consecutive days, of 5 drams of a 2 per cent. solution.

The Treatment of Tachycardia.—HAY (*Allgemeine Wiener medizinische Zeitung*, 1907, xiii, 142) considers that treatment can influence the progress toward recovery from tachycardia but little. At times the attacks increase in number as age advances, sometimes they decrease; nevertheless, treatment may lessen the patient's discomfort to a considerable degree. To diminish the number of the attacks we should endeavor to restore the normal cardiac regularity, and to attain this end we should employ general tonic treatment, all mental and physical overexertion should be avoided, and the mode of life should be regulated. All intes-

tinal, uterine, and renal difficulties which may produce reflex excitation should be corrected, and the digestion, in particular, should be regulated. Coffee, tea, tobacco, and alcohol should be forbidden and, during attacks, rest and light diet should be enjoined. In nervous subjects the bromides are useful and the attacks may be shortened by various means. For example, the patient should press his arms and elbows strongly against his chest, compressing the abdomen at the same time, while he holds his breath after a deep inspiration. Good results are obtainable by means of deep, forced respiration, which tends to reëstablish normal heart action. Digitalis is often used, and some consider that it should be given in large doses; it is, however, not always able to give relief. If there is stasis in the portal or general venous circulation, calomel and saline purgatives are indicated. Morphine and applications of ice or sinapisms to the precordium should not be employed unless there is marked cardiac distress. The blood pressure should be carefully watched; during an attack the venous pressure increases and that in the arteries becomes less. Should the arterial pressure be elevated the hippurates, benzoates, and nitrites are indicated. Calcium chloride should be given if the vascular contractility is irregular. As a whole the treatment of this condition is empirical, and we should endeavor to find a drug or combination of drugs which is capable of lessening the excitability of the auriculoventricular band of muscular fibers.

The Treatment of Dropsy by the Deprivation of Salt.—HADFIELD (*The Practitioner*, 1907, vi, 821) considers that there are three theories upon which this form of treatment is based, and which, of the many which have been advanced to explain the efficacy of this therapeutic measure, are worthy of special attention. They are as follows: (*a*) The retention of chloride in kidney disease is due to the morbid condition of the kidney itself, a condition which leads to relative impermeability of the organ to chlorides. (*b*) The second theory maintains that the retention is a simple physical process, entirely secondary to the retention of water in the body. (*c*) The third theory holds that in dropsical patients the body tissues are in some way altered, so that they are enabled to hold, in combination with themselves, a larger amount of salt than usual. These theories are discussed *pro* and *con* and the author states, concerning three patients suffering from ascites and one affected with chronic nephritis, who were treated alternately on saltless and salt containing diet, that in each instance it was found that deprivation of salt seemed to exercise a beneficial effect, not so much in dispersing the fluid as in delaying its accumulation. The results obtained were less successful than have been obtained by this means in France, but the benefit accruing to the patients was quite sufficient to justify the employment of this method of treatment.

Opsonins and the Specific Treatment of Tuberculosis.—SQUIRE (*Brit. Med. Jour.*, 1907, i, 1417) holds that it appears, with our present knowledge, that in those diseases (such as tuberculosis) in which the bacteria produce endotoxins and which are, for a time at least, localized, injections of toxins may be useful in prophylaxis, but are of little use in

the actual cure of the disease. He is still unconvinced of the wisdom of attempting to cure pulmonary tuberculosis by the introduction into the body of a further supply of tuberculous toxin. The procedure seems too risky with our present incomplete knowledge of the formation of antibodies and of the conditions which regulate the specific protective action of the leukocytes. Tuberculin may be a valuable adjunct in the treatment of surgical tuberculosis and possibly in tuberculosis of internal organs other than the lungs, but it is inapplicable in pulmonary tuberculosis. Three patients are cited in whom tuberculin treatment administered with all the precautions elaborated by Wright appeared to light up quiescent mischief in the lungs. In conclusion, Squire states that he fears that we have not the cure for consumption in tuberculin, even when regulated by watching the opsonic index, but it seems possible that we are almost within measureable distance of a satisfactory specific treatment for tuberculosis, and that we are indebted to Wright for much of our progress toward this desirable goal.

Tannin in Bronchiectasis.—MARINI (*Jour. des Practiciens*, 1907, xiv, 219) finds that tannin and calcium biphosphate exercise a marked vasoconstrictor action upon the pulmonary tissues; they also modify and deodorize the purulent expectoration. He prescribes four powders daily, each containing 4 grains of each drug. If hemoptysis takes place the quantity of the tannin may be increased by one-half. During the treatment the patient should drink only water, for all other liquids, especially alcohol, are contra-indicated.

The Treatment of Asthmatic Attacks.—VON DEN VELDEN (*Münch. med. Woch.*, 1907, xiv, 697), on the ground that theobromine sodiosalicylate possesses a dilator action upon the vascular system, has employed this drug in a number of patients affected with bronchial asthma. His results are most encouraging. He has also used the drug in asthmas of the so-called nervous type and in the catarrhal form of the affection. At the inception of the attack he prescribes 15 grains dissolved in water; if relief is not apparent in fifteen minutes a second dose is given; rarely is a third necessary. In most instances the condition is much ameliorated and sometimes the attack is terminated entirely No tolerance to the drug is established and it may be taken daily for a considerable period. Renal and circulatory lesions may contra-indicate its administration.

The Treatment of Exophthalmic Goitre.—CZYHLARZ (*Wien. med. Presse*, 1907, xi, 413) considers rest an important factor in the treatment of this condition, especially when emaciation is a marked symptom. Exercise and high altitudes should be avoided and the sea-side does not agree in some instances. Carbonic acid gas baths and chalybeate and carbonic acid waters are often useful. Other hydrotherapeutic measures which sometimes are beneficial are packs and sprinkle douches. An ice-bag may be applied to the enlarged thyroid gland and galvanization of the sympathetic nerve may be undertaken. Iron is especially indicated if chlorosis is present, and the preparations of digitalis may be employed to combat the tachycardia. Quinine and arsenic are sometimes useful as tonics, and sodium phosphate has been recom-

mended by Kocher. Iodine should not be given, but the bromides may be prescribed as symptomatic remedies. Antithyroid medication gives varying results, and the same is true of the administration of thymus extract. With regard to operation it may be said that resection of the sympathetic nerve is useless, but partial thyroidectomy may bring about a cure. Sorgo reports 30 per cent. of recoveries, 51 per cent. of ameliorations, and 13 per cent. of deaths. Radiotherapy has been advocated and has caused improvement in some instances; it is especially potent in bringing about an increase in weight. In conclusion the author states that the most valuable form of treatment is partial thyroidectomy.

PEDIATRICS.

UNDER THE CHARGE OF

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Cerebrospinal Meningitis of the Apoplectic Type, with Hyperpyrexia.—H. F. WARNER (*Brit. Med. Jour.*, 1907, i, 992) reports the case of a girl aged ten, who previous to onset had been quite well. While at school she vomited once without apparent cause; later in the day she complained of pain under the left jaw, where there were some enlarged glands, but nothing was thought of it until later, when she suddenly fell from her seat in a convulsion. She remained stuporous from then on until death. Examination showed dilated, equal pupils, retracted head, rigidity of neck and limbs, increased knee-jerks, bilateral Kernig's sign, dissociated eye-movements and divergent strabismus, clenched hands, with occasional bilateral convulsive movements, knees drawn up and other joints flexed. Breathing was stertorous and rapid, pulse 148, temperature 98°. The next day the knee-jerks had disappeared, the Babinski reflex was present, the stupor had deepened, and the temperature rose to 104°. An examination of the eyes showed slight optic neuritis, and a lumbar puncture resulted in the withdrawal of clear fluid, from which was cultivated a large Gram-positive coccus, but no meningococcus. She had two convulsions during the day; in these she became markedly cyanosed, her respirations increased to 85, her temperature rose to 106,° and her pulse could not be counted. She died shortly after the second convulsion. There was no definite rash, but an evanescent, erythematous mottling of the skin could be observed for a short time. The whole illness occupied only 37½ hours. The autopsy showed markedly engorged meninges, but no thickening of membranes or exudate; no gross change could be found in the brain. The spinal cord was surrounded by a clear, gelatinous material. The spleen was enlarged, as were also Peyer's patches and the lymphoid follicles of the intestines; the thymus also was large. There were no signs of tuberculosis anywhere. Warner considers this a case of meningitis, the organism producing it having been of such virulence as to have caused death before the usual exudate had time to form. The optic neuritis also must have been toxic.

Thrush and its Severer Effects.—In the space of ten years J. GORDON SHARP (*British Journal of Children's Diseases*, 1907, iv, 292–296) has seen 7 children dying from thrush as a primary affection. The average age at death was eight and a half weeks, and none was over thirteen weeks. The immediate cause of death in 3 instances was laryngeal implication; in the other 4 progressive wasting, with vomiting and diarrhœa. The fatal cases occurred among people who may be termed "dirty," but the disease occurs in well-to-do circles as well. Families living near ash-pits seem to furnish more cases than those living a distance from them, and improved sanitation has diminished the number of cases in the last few years. Summer diarrhœa is found more frequently among children who have or have had thrush, and Sharp is of the opinion that the Saccharomyces albicans is the cause of it in such instances. Rarely does the fungus grow in the intestines, but the diarrhœa and soreness are due to decomposing food, fungus, and tissue carried down. The treatment of thrush consists in general and local measures. The former consists of castor oil to clear the intestines, a thorough cleansing of the bottles, and dilution of the food to 1 part of milk to 3 of water; whey or weak beef-tea should be given in cases of diarrhœa. The local treatment is attended to by the physician himself. A clean, soft rag is wrapped around the handle of a teaspoon dipped in warm water, and the entire surface is cleansed of fungus and adherent matter until it bleeds. Powdered boric acid is next applied to every part of the mouth; the same procedure is then gone through with the nasopharynx and the epiglottis, if necessary. The nipples and the breasts of the nursing mother must be washed off with clean, warm water twice daily. If the external ear is implicated carbolic soap must precede the boric powder.

A Peculiar Outbreak of Erythema Nodosum.—W. LANGFORD SYMES (*British Journal of Children's Diseases*, 1907, iv, 281–284) reports an epidemic of erythema nodosum, occurring in one of the Homes for Children. The house was large, airy, detached, and had apparently good sanitation; there was very little overcrowding, and there was nothing peculiar in the food of those affected. There were 13 cases in all; 1 of them was followed within twenty-four hours by symptoms of meningitis, and death followed two and a half days after the onset of the erythema; another patient became profoundly ill, temperature going to 104°; 4 developed endocarditis as a part of the infective process; 4 of them had relapses. The outbreak emphasizes the following facts: erythema nodosum may become a serious and dangerous disorder; it is sometimes epidemic; it appears to be of an infective nature; endocarditis may arise during its course; it may be quickly followed by meningitis.

The Medical Treatment of Congenital Pyloric Stenosis.—SUTHERLAND (*Lancet*, March 16, 1907, i) refers to the medical treatment of this affection by means of dieting and gastic lavage. He reports 3 cases which he has treated successfully by such measures. He insists that there will be fewer and fewer cases in which surgical interference will be called for, as our knowledge and experience of the medical treatment advance. The first sign of progress toward cure is cessation of the vomiting. This usually follows quickly after lavage and suitable

feeding have been carried out. Then the bowels begin to act naturally. This is a very important sign of progress, for it is in such marked contrast to what occurs in untreated cases. After the medical treatment has been begun the bowels act two or three times a day without artificial stimulation, and the motions are larger and consist of fœcal matter. The stomach peristalsis gradually becomes less marked, and eventually passes off completely. The discomfort and constant whining of the infant also cease. The infant's nutrition improves. This is manifested by a healthier color, increased activity of the limbs, and by a slow gain in weight. These infants cannot be fattened rapidly. Any attempt to secure this will probably end in disaster. A simple diet is best, and the less weighing of the child the better, especially if anxious relatives are about. Diarrhœa is a common complication in the course of treatment. It is due to the fact that the bowel is unused to the presence of food material, and so is easily irritated at first. Diarrhœa is always a serious symptom. Sutherland has not derived much benefit from the administration of antispasmodics, or of opium, even when pushed to their full physiological extent. Saline injections, however, he finds of great service in marasmic babies. From 4 to 10 ounces of normal saline solution can be given daily, and will act as a restorative until the improvement of the pyloric function allows of the entrance of a sufficient amount of fluid into the system by the natural channel. Brandy is also of use as a stimulant. Inunctions of cod-liver oil may be of some value, but in the only case in which he employed it in this way it caused a skin eruption.

Pneumothorax and Acute Hemoptysis in Children.—O. Cozzolino (*La Pediatria*, 1906, 881) described two such cases which occurred in the children's clinic at Genoa. In the first there was a localized tuberculous infection of the tracheobronchial and mesenteric glands in a girl aged twenty-eight months; tuberculous infiltration of the left lung and pneumothorax of the same side. The author gives a tabular analysis of 41 cases: Pneumothorax is very rare in children and is always secondary; tuberculous pneumothorax is, in contradistinction to adults, less frequent than all the other forms of pneumothorax taken together; only about 40 per cent. of cases of pneumothorax in children are tuberculous, the majority of the cases being consecutive to abscess, gangrene, pulmonary infarct, traumatism, etc.

Diagnosis is often difficult owing to either the insidious onset or the absence of important symptoms (amphoric breathing, metallic tinkling, etc.), or to the difficulty of obtaining them in a child that breathes badly. Some of these symptoms, moreover, may be met with in children having pulmonary cavities, pleurisy, or pneumonia.

The cause of infantile tuberculous pneumothorax is either the rupture of a pulmonary cavity by progressive thinning of its walls or the pressure on the lung exerted by masses of swollen, caseous bronchial glands, or more rarely the rupture of an emphysematous vesicle. In Cozzolino's case there was perforation of a large tuberculous cavity in the lower lobe of the left lung, which could not be diagnosticated during life.

Prognosis is absolutely unfavorable, linked as it is with that of the causative disease which contributes to a fatal issue. The most common site for perforation is the base of the left lung. Infantile pneumothorax,

whether tuberculous or not, is invariably total and rapidly becomes a pyopneumothorax.

The second case described was a profuse and rapidly fatal hemoptysis in a girl, aged four and a half years, affected with chronic miliary tuberculosis, with bronchopneumonia and a cavity in the left apex. A tabular analysis of 48 cases occurring in children below the age of seven years is given, which demonstrates that profuse and fatal hemoptysis due to tubercle below seven years of age is extremely rare, and occurs only in advanced stages of the disease; there is always a cavity of the lungs, or of the tracheobronchial glands; it is often of a fulminating type, without premonitory signs; its extreme rarity is partly explained by the fact that tuberculosis of the lungs in young children produces hepatization and vascular occlusion rather than destruction of tissue and formation of vomicæ.

OBSTETRICS.

UNDER THE CHARGE OF

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Eighty-eight Cases of Early Tubal Gestation.—HAMILTON BELL (*Jour. Obstet. and Gyn. Brit. Empire*, December, 1906) gives the results of his studies in 88 cases of tubal gestation at St. Thomas' Hospital. Only early cases are taken and those under the care of physicians sufficiently experienced to study them accurately. The series is tabulated and the cases are subjected to analysis. Attention is drawn to special points of interest in the various cases. Bell concludes that the diagnosis of tubal gestation followed by rupture or abortion is difficult. In many cases the patient has been ill for one or two months before coming to the hospital, the condition not having been correctly diagnosticated.

Typical signs and symptoms are, the missing of one or two menstrual periods, sudden acute pain in the lower portion of the abdomen on the right or the left side, with faintness and vomiting. At about the same time vaginal hemorrhage occurs, continuing irregularly, the blood lost being usually less than that of normal menstruation. Clots are often passed, and sometimes a cast of the uterine cavity; there is slight elevation of temperature and difficult micturition. When rupture and internal hemorrhage have taken place there will be characteristic symptoms of bleeding. In the majority of cases the hemorrhage is only sufficient to form a pelvic hematocele.

The signs characteristic of this condition are the pushing forward and to one side of the uterus, the cervix being softened and the body of the womb slightly enlarged. Between the uterus and one side forms an elastic swelling which depresses the cul-de-sac in the roof of the vagina, which varies in consistence and tenderness. In 50 per cent. of the 88 cases a period of amenorrhœa occurred, lasting for five weeks or more. In all of the cases abdominal pain was pronounced. It was acute, with faintness and vomiting, in 21; acute with faintness only in

19; acute with vomiting only in 21; acute with faintness or vomiting in 11, and indefinite abdominal pain in 15. The hemorrhagic discharge from the vagina occurring at some period of the illness and persisting was a very constant and important symptom. It was present in 73 out of the 88 cases. The passage of a decidual cast was a very uncertain and misleading symptom. In only 17 of the 88 cases was there a clear indication of this occurrence. Elevation of temperature was present in but 23, but this is unquestionably too low an estimate for a careful observation, and this symptom was not afforded in many cases. It is of little value in differential diagnosis. Disturbance of the bladder was present in 20 of the 88 cases. These cases show that no reliance can be placed upon the occurrence of a period of sterility preceding the ectopic gestation. As regards age, the accident is most frequent between the twentieth and fortieth years. The physical signs varied with the degree of hemorrhage and the source of the bleeding. The condition of the breasts was extremely misleading, while the presence of a pelvic mass was of more value in diagnosis. Softening of the cervix and enlargement of the body of the uterus often gave information concerning the nature of the pelvic swelling. Experienced observers could detect the persistence of the pelvic mass, which was suggestive. Physical signs alone cannot be exclusively relied upon to make a diagnosis. The clinical phenomena must be thoroughly studied and compared. Especially important is the persistence of irregular bleeding. Abdominal pain in the lower portion is next in value. As far as treatment is concerned, most of these cases were treated by surgical operation as soon as the diagnosis was made. Some were treated by rest only, but these were the milder cases in which a positive diagnosis was not possible. When a pelvic hematocele had formed the wishes of the patient and the circumstances of her life should be carefully considered. In the majority of cases recovery will follow whether the treatment is surgical or expectant. Champneys reports 75 cases, in only 26 of which operation was done. As this was reserved for the most severe cases, it was attended by high mortality. In the whole series 7 died, all of them after section, giving a mortality of 27 per cent. In Bell's series of 88 cases, most of them treated by operation, there were 3 deaths with a mortality of 3.4 per cent.; 73 of these were treated by abdominal section, including all the most severe cases. This makes the mortality rate 4.01 per cent. As regards the convalescence of the patients, it is thought that the number of days spent in the hospital, in the cases operated upon, and those not operated upon, is not an accurate criterion. In the first half of the series, the average convalescing was 35.3 days; in the second half, 29.4 days. In Champneys' series the average hospital convalescing was 39.2 days. The mortality was least in those patients operated upon as soon as possible after admission.

This paper and that of Champneys are tabulated and compared in that form. Champneys' patients were largely treated by the expectant method. His mortality was 9.3 per cent., while Bell's mortality was 3.4 per cent. In Champneys', 45.3 per cent. of the patients recovered without operation; in Bell's, but 10.2 per cent. Champneys practised vaginal section in 20 per cent., while Bell could collect but 6 vaginal sections in his cases. The mortality of abdominal section in Champ-

neys' cases was 26.92 per cent.; in Bell's cases, 4 per cent. This striking disparity would indicate that early operation is by far the safer procedure.

Ectopic Gestation Occurring in India.—STANDAGE, of the India Medical Service (*Jour. Obstet. and Gyn. Brit. Empire*, December, 1906), describes 15 cases of ectopic pregnancy occurring in India; 5 of the 15 were European women; the remainder were natives. The ages of these patients ranged from 43 to 22 years. There was but one primipara. The average number of previous pregnancies among these patients was 3.06 per cent. and among the 14 women who had previously been pregnant an interval of 6.07 years had elapsed. But 3 abortions or miscarriages among these patients were recorded.

As regards the signs of ectopic gestation, all but one patient described had distinctly disordered menstruation. On the average 2.2 months passed. Among the signs of ectopic pregnancy there was no nausea or morning sickness. The presence of milk in the breasts was noticed in 4 cases, and 6 had pelvic pain which became sudden in 11. The effect of the pain was not as pronounced as has been reported by some. In fact, among the natives, acute symptoms were comparatively rare. Even after rupture of the pregnant tube the patient would continue about for some time before yielding to the illness. From twenty days to two months was observed as the interval between the onset of pain and the patient's giving up to the condition. In one case a native woman had hemorrhage sufficiently large to fill the pelvis and a portion of the abdomen with blood clot. For a month after the first symptoms this patient worked as usual, and was finally compelled to seek medical advice because of a swollen abdomen. Upon operation the abdomen was filled with blood clot, and a ruptured sac of five months' pregnancy and fœtus were discovered in the peritoneal cavity.

In every case except one in which rupture of the Fallopian tube was either suspected or present, there was a history of a sudden attack of pain. In native patients this pain was never described as agonizing. There was constipation or painful movements of the bowels, and frequent emptying of the bladder when much blood was brought into the pelvis. One patient came to the hospital principally to be relieved of disturbance of the bladder.

The most constant symptom present in all cases but one was irregular hemorrhage, together with a thick, glutinous, reddish or brown discharge. This begins with the expulsion of the uterine decidua, which is usually thought by patients to be a miscarriage. This oozing of blood continues until the condition is permanently cured by operation; 5 out of 15 patients gave a history of abortion occurring at periods varying from four to eighteen days before admission to the hospital.

The detailed report of these cases illustrates how wide is the variation in symptoms and how obscure many of these cases are. The most significant symptom uniformly found was tenderness of the abdomen. This occurred in 100 per cent. of the cases. A tender pelvic tumor was found in 93.3 per cent.; irregular, more or less abundant hemorrhage was also noted in 93.3 per cent. In the majority of cases there was cessation of normal menstruation, and a sudden attack of pain more or less severe. Disturbance in the function of the bladder, vague pelvic pains, and painful defecation occurred in two-fifths of the cases.

A history of abortion with probably the expulsion of a decidual cast was given in one-third of all cases. Milk was found in the breasts in one-fourth of the cases.

As illustrating the tolerance of the Indian native to ectopic gestation and rupture, collapse occurred in but 21.4 per cent. The remainder of these patients did not even go to bed. In none of the cases was there morning nausea and vomiting. The death rate of the series was 7.1 per cent., the fatalities occurring in cases which had become septic, and in cases in which operation was declined.

The Neutrophiles of the Blood in the Puerperal Period, and the Effect Produced by Antistreptococcic Serum.—BURKHARD (*Archiv f. Gynäk.*, 1906, Band lxxx, Heft 3) reviews Arneth's work upon this subject. Early in the puerperal period an increase in leukocytes is observed, especially in the cells having a single nucleus. In a case of fatal postpartum bleeding a great increase in the leukocytes to 45,000 was observed; in a case which recovered the number was 15,000. Twenty-four hours later it had fallen to 6000. In pregnancy complicated by nephritis and by lesions of the heart the neutrophiles are not changed. In septic infection there is increased leukocytosis, as a rule, but not as typically and as pronounced as in pneumonia. In puerperal sepsis the number may vary from 2400 to 28,000. In fatal septic cases 2600 to 3500 with 70 per cent. of single nucleus young cells, has been observed. In severe toxemia as few as 2400; and in septic cases, which recovered, 4000 to 5000 have been observed. In fatal pyemia 1800 to 7500 leukocytes are recorded. Other cases with polyleukocytosis ranged from 12,000 to 28,000; polyleukocytosis is an important and significant symptom. In 11 cases of severe infection with streptococci, the number ranged from 6000 to 9000; in 4 cases in which saprophytes, or the bacterium of the colon were present, the number was 18,000 to 28,000. When the septic infection fails to become localized the number of leukocytes is least; when localization becomes established in streptococcic infection, the leukocytosis rises to 12,000 to 15,000; in cases not of streptococcic infection it may rise to 24,000. When improvement begins the leukocytosis decreases. Paultauf's antistreptococcic serum produced improvement in 60 per cent. of the streptococcic cases in which it was used. The serum increased the leukocytes and neutrophiles.

GYNECOLOGY.

UNDER THE CHARGE OF

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A Special Form of Climacteric Hemorrhage.—H. MEYER-RUEGG (*Zentralbl. f. Gyn.*, 1907, xxxi, 629–632) remarks on the greater frequency with which women, flooding irregularly about the time of the menopause, consult physicians. He reports the cases of 4 women, all of whom were passing through the climaceteric period, and who came to

him because of prolonged serosanguinolent discharge; in several of them it had lasted continuously for weeks. In all of them he found the following conditions: The menstruation had always been profuse and had lasted long; because of this and the profuse leucorrhœal discharge complained of, a preceding state of endometritis could be believed to have existed. The examination showed a smooth, atrophic vaginal mucous membrane; the vaginal part of the cervix was small or entirely absent; the supravaginal part relatively large and the corpus uteri small, hard, and partly involuted. The cervical os was very small and in 2 cases it could only be distinguished because of a thread of mucus hanging from it. After some difficulty a sound could be introduced and the cervical canal was found ballooned out. Dilatation of the cervix brought about an escape of loose, black coagula. He considers the condition one of "cervical hematometra" and believes it to be caused by the prolonged retention of blood behind the small external os. The removal of the stenosis by dilatation or discission brought about a definite cure in each case.

Unexpected Cures in Inoperable Carcinoma of the Uterus.—Unexpected cures in inoperable carcinoma of the uterus are very rare, as are also cases in which for a prolonged period of time no recurrence is noted. Czerny has only been able to report one such. F. WEINDLER (*Zentralbl. f. Gyn.*, 1907, xxxi, 632–635) reports the details of 3 such instances, in all of which the patients seemed hopelessly doomed and in which they recovered against all expectation. All are living today, five years without a recurrence having been reported. The procedure in all was thorough curettement, cauterization, and application of concentrated carbolic acid. Weindler emphasizes as necessary conditions for such a cure: the full protective forces of the organism against the proliferation of the tumor cells. These are round-cell infiltration in the stroma, increase in the number of bloodvessels in the neighborhood of growing carcinoma, the destructive power to carcinoma toxin of the mastzellen in the lymph glands, and the thickening of the cervical epithelium. Other favorable moments for a cure by palliative measures are a certain degree of emaciation and thinness of the patient, deep action of the cautery, and a favorable histological structure of the tumor.

Extra-uterine Pregnancy.—Between the years 1878 and 1905 RIEDINGER (*Wien. med. Presse*, 1907, xlviii, 20, 21, and 22) observed among 28,000 patients 42 individuals with extra-uterine pregnancy and 79 with retro-uterine hematocele, altogether 121 cases. Of the former he operated on 14, with 1 death; of the non-operated cases 3 died. Of the 79 hematocele patients 9 were operated on, also with 1 death, while of the other 70 none died. In spite of the relatively favorable results of the conservative measures Riedinger declares himself, because of the finished state of our modern operative technique, in favor of active interference as soon as a diagnosis is made.

Uterine Inversion Following an Abortion.—F. PREISMANN (*Zeit. f. Geburt. u. Gyn.*, 1907, lx, 152–160) reports the case of a woman, who had previously given birth to 5 children, and in whom without known cause a miscarriage was noted about the fifth month of her

sixth pregnancy. The fœtus came away easily, but the placenta remained behind. The patient bled profusely during the next few weeks, but she did not send for a physician until a month later, when after lifting a heavy trunk the uterus suddenly inverted. The placenta was easily loosened then, but the hemorrhage which followed was so great as to cause the death of the patient. A microscopic examination of the uterus revealed marked degenerative changes in the muscle of the uterus about the point of placental attachment. Preismann believes that the placenta, which in none of the reported cases was expelled before the inversion of the uterus, plays a role in the production of the inversion by pulling on the weakened uterine wall; no special violence is needed to bring it about.

Destructive Vesical Mole.—H. KAUFFMANN (*Zeit. f. Geburt. u. Gyn.*, 1907, lx, 136–152) reports the case of a woman of thirty-eight, who had given birth to 11 children, with all of whom she had considerable difficulty because of her flat pelvis and the large size of the infants' heads. Her menstrual flow had always weakened her, but never so much as since the birth of her last child. Because of a persistant bloody discharge she was examined and a diagnosis of vesical mole made; a few small vesicles came away after manual dilatation of the cervix. Curettement was easy and followed by immediate improvement; the patient recovered apparently very promptly. A recurrence was noted within a month and a second curettement resorted to; it was thought to have been a retention, as only a small amount of mole material could be found. Within a few months the patient developed to the right of the uterus a soft elastic tumor, which was believed to be a chorion epithelioma growing from the uterine tissue, but upon operation it was found to be a vesical mole the size of an orange, which had developed in the veins of the broad ligament. It was connected with the uterine cavity and a polyp growing from it by a small pedicle; otherwise the entire organ was absolutely distinct from the tumor. This new hydatiform growth showed no essential difference from the primary growth, but was limited to the different layers of the veins; it must therefore be looked upon as having arisen from the previously removed uterine mole (being a direct continuation of it), and as it extended beyond the limits of the uterus, it has to be classed with the type known as "destroying vesical moles." On account of the limitation of this mass to the broad ligament, the other structures of the pelvis not having been affected at all by it, the tumor is a further proof of the fact that vesical moles may be followed by benign formations in the pathological conception. Such tumors may become malignant at any time, but do not usually become malignant until some new irritant, such as pregnancy, is added. Four months have elapsed since this last operation, but the author is not sanguine as to the definite recovery of his patient.

Chorion Epithelioma Developing Between the Layers of the Broad Ligament.—A. GARKISCH (*Zeit. f. Geburt. u. Gyn.* 1907, lx, 115) reports from Franque's clinic the case of a woman of thirty-seven, who had previously given birth to two healthy children. Within two months she had repeatedly had profuse bloody discharge from the genitalia and was admitted to the clinic because of its continuation. The

examination revealed a hard, nodular tumor rising from the left side of the pelvis and another on the right side connected therewith. The operation revealed the mass to be a chorion epithelioma of the left parametrium. The patient died twenty-four days after the operation, of pulmonary embolism, metastases to lung, and pulmonary abscess; metastases had also appeared in other parts of the body, a recurrence being noted also in the pelvis. A careful macroscopic and microscopic examination of the mass produced the following facts and led to the deductions recorded. The case was one of chorion epithelioma which had developed between the layers of the broad ligament and without affecting the uterus. It was most likely preceded by a tubal pregnancy at the isthmus. The tumor developed after the rupture of the tube, from the tubal surface nearest the broad ligament; it developed by growing into the layers of the ligament, separating them as it developed. The possibility of an ectopic chorion epithelioma following an intrauterine pregnancy and miscarriage is not denied. The central portion of the Fallopian tubes showed marked decidual change; the uterine and abdominal portions showed none at all. The uterus presented a typical decidua, 1 cm. thick; the surface epithelium of this had markedly flattened and had proliferated into several layers; the glandular epithelium also showed remarkable proliferation. There were decidual changes on the surface of the ovary. The case belongs to the most malignant forms of chorion epithelioma, as the tumor was found extending into the abdomen within a few weeks after the last period and death occurred four months after the last menstruation.

OTOLOGY.

UNDER THE CHARGE OF

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The Operative Treatment of Othematoma.—H. SELIGMAN'S (*Archiv. f. Ohrenheilk*, 1907, vol. lxix) operative treatment differs from the ordinary treatment, by means of simple incision and pressure dressing, in that it aims at a radical procedure in excision of the diseased cartilage, with retention of the protective healthy skin. The auricle having been made surgically clean, and anesthetized by subcutaneous injection of a solution of cocaine and suprarenine (solution of cocaine muriate 0.05 to 10.0 + suprarenine 10.0 to 10 solution, minims 2 to 3), an incision is made throughout the length of the swelling on the anterior surface of the auricle, in its long axis, but through the skin only. There is usually but little hemorrhage, and the two skin flaps thus formed are successively seized by the forceps, dissected up from the underlying swelling, and retracted until the contour of the swelling is completely exposed; a small short-bladed scalpel is the best instrument for this dissection and extreme care should be taken to avoid puncturing the underlying sac, as the lack of the smooth resisting surface which it presents, when intact, considerably increases the difficulty of preparing a perfect skin flap. With the skin flaps completely retracted. and held in position by means of

blunt hooks, a circular incision is made about the base of the swelling, and the tissues covering the fluid contents of the sac completely excised. With the evacuation of the fluid there then remains only a concavity upon the surface of which the skin flaps may be adjusted and kept in place by the pressure of gauze pads, until healing has ensued, the ultimate result being a smooth skin surface, with a slight linear scar on the anterior face of the auricle, and a preservation of the natural contour.

This method of operation is equally applicable in the perichondritis of the auricle which sometimes occurs as a consequence of the tympano-mastoid exenteration. It is important, however, to distinguish between the serous and the suppurative form of this affection: in the latter the flap operation is sometimes ineffective, in the former it is always applicable; the incision through the skin here also should be made over the greatest convexity of the swelling, in a line with its long axis. Of the 11 cases, upon which Seligman has operated by this method, all have been done upon the anterior face of the auricle.

Microscopic examination of the excised outer covering of the othematoma justifies its radical removal and explains the deformity which usually results in unoperated cases; this outer covering is mainly cartilage, isolated from the main body of the cartilaginous plate of the auricle by means of cicatricial tissue, broken up into individual portions, inelastic, disorganizing and functionally ineffective for the preservation of the contour of the auricle. In cases of spontaneous healing the cicatricial retraction of the connective tissue fibers, evident in the covering of the othematoma, by exertion of varying stress in different directions, under shrinking of the connective tissue coincident with resorption of the fluid contents of the swelling, contribute to the irregularities of surface pertaining in a deformity of the auricle which the method of operation above described is calculated to avoid.

Mastoiditis and Thrombophlebitis of the Lateral Sinus.—E. BARDIER and E. MERIEL (*Annales des maladies de l'orielle et du larynx*, 1906, xxxii, 140). The early diagnosis of thrombophlebitis of the lateral sinus and jugular vein is one of the important problems of otology today, and any experience which will tend to enlighten the profession upon the clinical evidences of definite pathological changes is worth recording. Bardier and Meriel report a very interesting case of parietal thrombus of the sinus which was suspected but not proved until autopsy. The clinical history and the autopsy findings afford an opportunity for important practical deductions regarding the recognition and treatment of this class of cases.

A young woman, aged twenty-one years, with a history of chronic suppurative otitis media involving the right ear, of eight years' duration, was suddenly attacked by severe pain in that ear, with high fever and rapid pulse. Antipyretic treatment did not relieve the general condition and four days later, when she entered the hospital, the temperature had risen to 105° F., the head pain was severe and she had experienced chills and nausea. Pus from the auditory canal gave a pure culture of the pneumococcus. The right sternocleidomastoid muscle was contracted and painful, but the examiner could not determine any induration along the course of the jugular vein. The patient's general appearance was

that of a serious infection, probably arising from invasion of the lateral sinus. Mastoidectomy was performed promptly and the antrum cleared of the necrotic material, but the sinus was not exposed, apparently because the operator had not discovered a direct carious track to that vessel. The temperature immediately fell to 99.5° F. and varied but slightly for two days, but on the third arose again to 105°, with chilliness and vomiting. Then began the typical zigzagging temperature curve, from 100° to 106° F., and a second operation was advised. This time the dural covering of the sinus was exposed, after an exploration of the temperosphenoidal lobe for extradural abscess or meningitis, but, inasmuch as the vessel seemed to present a normal color and was compressible, it was not attacked. The septic course continuing, a third exploration was performed three days later but, still, in spite of the clinical evidences of thrombosis, the surgeon could not persuade himself to open or ligate an apparently normal vessel. Two days later, the ninth from the date of entrance, the patient died of general septicemia.

Autopsy disclosed the fact that the lateral sinus and jugular vein, from the torcula to the hyoid bone, was the seat of a parietal coagulation, 3 to 4 mm. in thickness, covered with purulent streaks; about three-quarters of the central lumen of the sinus was permeable. At the base of the right lung three metastatic abscesses were found and there were areas of bronchopneumonia.

Bardier and Meriel draw the salutary conclusion that it would be wiser in such cases to follow the general clinical indications than to rely upon the appearance of the vessel wall. A study of the temperature is of far more value than mere inspection of the vessel or a drawing of blood from its lumen; in this instance, free blood might have been obtained, despite the presence of an extensive thrombus. Success in the treatment of lateral sinus thrombosis depends upon its early recognition and the prompt establishment of a barrier between that thrombus and the heart. When considering the graver sequels of the suppurative otitis media we must remember that a zigzagging fever curve, especially when accompanied by chills, points more strongly to sinus thrombosis than to any other of the possible complications, and, furthermore, when a sinus has been exposed, because the clinical evidence pointed strongly to infective thrombosis, it is more conservative to ligate the jugular and open the sinus, than to leave it alone.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Biology of Diplococcus Intracellularis.—FLEXNER, (*Jour. Exp. Med.*, 1907, ix, 105) presents a number of new facts in regard to the biology of Diplococcus intracellularis, especially in regard to the autolysis of the

organism. The effect of a number of experimental conditions was tried upon the viability and dissolution of this organism outside of the body. Flexner found that the brief vitality of the cultures outside the body is not to be ascribed directly to the exhaustion of the medium or the accumulation of injurious products of growth. Cold favors destruction of the organism on solid media and in salt solution suspensions. But cold is more injurious to the cocci and destroys them more quickly in a weak than in a highly concentrated suspension. 2° C. was the temperature used. When a similar series of concentrations of suspension of the organism was kept at 37° C., it was found that more organisms survived in the weaker than in the stronger suspensions, giving opposite results from those obtained at 2° C.

When Ringer's solution was used instead of normal salt solution, the organism remains alive in suspension much longer. This fact is probably due to the influence of the calcium salt. Normal salt solution is directly poisonous to Diplococcus intracellularis, and it is apparent that the toxic effect of the sodium chloride can be neutralized by the calcium and potassium salts in Ringer's solution.

Disintegration of the organism occurs rapidly in salt solution suspension, and this is apparently due to an intracellular enzyme. It was found that toluol, which kills the cells but which does not prevent enzymic action, hastened disintegration. Suspensions heated to 60° C. undergo rapid disintegration, while heat of 65° or higher reduces the capacity of the diplococcus to undergo disintegration.

Potassium cyanide possesses the power of preventing or diminishing autolysis of the dead diplococci, thus agreeing with the findings of Jacques Loeb, that this substance has a restraining influence upon intracellular enzymotic activity. On removal of the cyanide the diplococci are partially restored to their previous state of autolysis.

This intracellular enzyme, which is apparently liberated when the cell is destroyed and can be obtained by washing the bacteria, was found to have a destructive action on other bacteria besides Diplococcus intracellularis. It is probable that non-Gram staining organisms are more easily disintegrated by the enzyme than are Gram staining organisms. This enzymotic action was not effected by toluol, but when heated to 65° C. it ceased to act on the diplococcus, while 70° C. was necessary to destroy its action for other bacteria.

Diplococcus intracellularis was found to have low and variable pathogenicity. Small guinea-pigs were found to be very susceptible, even more so than mice, to the same dose. After peritoneal injections there is a fall in temperature, and the extent of this fall is larger with virulent organisms and may be taken as an index of the degree of virulence. Within the peritoneal cavity the destruction of the organism is not dependent upon phagocytosis, but can occur in fluid inflammation exudates through self-digestion. Agglutination occurs in the peritoneal cavity. The diplococcus acts upon the guinea-pig by its intracellular toxin, liberated by disintegration of the organism and not by a secreted extracellular toxin. This is shown by the use of autolysates and cultures killed by heat. Autolysates are obtained by suspending masses of the bacteria in salt solution and then filtering or centrifuging until no bacteria remain. This fluid is toxic for small guinea-pigs when injected intraperitoneally. This toxic action is not materially reduced by heating the

fluid to 65° C.: when diplococci are heated to 60° C. their toxicity is distinctly reduced.

Among other lesions found in the guinea-pig were small hemorrhages in the peritoneum. As these might bear relation to the hemorrhages in meningitis in man they were investigated and found to be focal. The vessels were not injured or thrombosed, but the endothelium was sometimes destroyed, as may be seen after injections with hemorrhagin of snake venom. These focal hemorrhages follow injections of the autolysate, but more regularly with the centrifuged than with the filtered fluid.

Peritoneal exudate following injection of the diplococcus has in vitro a more destructive action than the blood serum from the same animal.

Absorption from the Peritoneal Cavity.—BUXTON (*Jour. Med. Research*, 1907, xvi, 17) continues his studies in absorption. The earlier part of the work, done in conjunction with Torry, appeared in the same journal, 1906, xv, p. 5, when the absorption from the peritoneal cavity and fate of inert particles and typhoid bacilli was discussed. The first part of the present paper deals with an attempt to determine the number of typhoid bacilli present in the blood of rabbits at various intervals after injection into the peritoneal cavity. The blood was found to contain many organisms immediately after large doses were introduced intraperitoneally, but at the end of one hour the number was greatly reduced, and in twenty-four hours practically no organisms were found in the circulating blood, although in some cases a few were found four days after the inoculation. In rabbits that succumbed to the inoculation many more organisms were found in the blood than in those animals which survived four days.

Organisms were found in various organs of rabbits that survived for four days, but they were present in the anterior mediastinal glands in much larger numbers than elsewhere, while in rabbits that succumbed to the inoculations the organs contained a great many more bacilli. In testing the bactericidal power of rabbit's serum, four days after inoculation, Buxton finds that this property is much less than it is in the serum from inoculated rabbits. The serum from normal rabbits varied in its bactericidal power inversely with the square of the dilution, that is, 1 c.c. of serum diluted 1 to 10, kills not one-tenth but, one-hundredth of the number that the undiluted serum kills.

In the seventh part of the whole series of papers Buxton describes the results of his experiments on the effect of minimal doses of bacteria, and discusses the bearing of these experiments upon the question of peritonitis. He finds that bacteria injected into the peritoneal cavity of experimental animals, even in minute doses, reach the circulation in a few minutes, and that this immediate absorption takes place by the lymphatics of the diaphragm.

He, therefore, thinks that his experiments indicate that the semi-sitting position of Fowler following operations for peritonitis is indicated in order to avoid a rush of bacteria to the diaphragm, and that flushing of the peritoneal cavity is contra-indicated. Buxton believes that the sudden death of rabbits following inoculations is due to toxemia, and that the deaths occurring within one or two hours after operations for peritonitis usually attributed to shock, are analogous.

The Changes in the Liver in Eclampsia.—Since Jürgens first described "hepatitis hemorrhagica" as a characteristic lesion of the liver in eclampsia, the condition has been repeatedly studied. Schmorl, in 1893, reported a study of 17 cases and in his descriptions distinguished between hemorrhagic and anemic necroses in this condition.

Konstantinowitsch (Ziegler's *Beiträge*, 1907, xl. 483) reports, from Marchard's laboratory, a study of the livers from 30 cases of eclampsia. He finds, as one of the earliest changes, alterations in the liver cells and of the endothelium of the capillaries in the peripheral part of the lobule. The changes, which consist in granulation and vacuolation of the protoplasm, increase as the disease proceeds until the liver cells present a reticulated appearance. One sees in all cases widening of the capillaries with congestion, and frequently escape of blood from the capillaries, in the peripheral part of the lobule. This is due to slowing of the circulation which is brought about directly by primary thrombosis of the capillaries in the periphery of the lobule. Konstantinowitsch lays great stress upon this thrombosis, and believes that the death of the liver cells goes hand in hand with the development and spread of the thrombosis. First the smaller and then the larger interlobular vessels are thrombosed. The thrombi are, for the most part, fibrinous, or composed of blood and fibrin, and are rarely if ever hyaline in character. In the neighborhood of the anemic necroses is found the fibrin which appears first in the periphery of the lobule and seems to precede the necrosis. Liver cells were found in the lumen of the portal and the hepatic veins, but this was considered to be an artefact. Under certain conditions these lesions, which are characteristic of eclampsia, may heal and give rise to a cirrhosis of the liver. In a few instances evidences of regeneration of liver tissue were seen, a process which before this time had not been noted in the lesions in the eclamptic liver.

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